DESCRIPTION

NOVEL ISOINDOLE DERIVATIVES

TECHNICAL FIELD

The present invention is useful in the medical field. More specifically, an isoindole derivative as a compound of the present invention exhibits an activity that achieves a high GLP-1 concentration in blood, and is thus useful as a therapeutic agent for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug.

BACKGROUND ART

The blood glucose levels of healthy individuals are controlled at a constant level by the action of insulin. Diabetes mellitus refers to a condition that chronically exhibits a hyperglycemic state due to a lack of this control, and a disease caused thereby.

The principal concept of the treatment of diabetes mellitus is to correct the hyperglycemic state, i.e., to return the glucose concentration in blood to a normal level. In recent years, it has particularly been recognized that an exceedingly important point for the treatment is how to suppress a sharp rise in blood glucose level after meals without influencing fasting blood glucose.

Main therapeutic drugs for diabetes mellitus currently used

in clinical practice are broadly classified into the following 3 types of therapeutic drugs, in addition to various insulin preparations. The first one is a drug group called insulin release drugs typified by sulfonylurea agents. These drugs decrease blood glucose levels by directly promoting insulin secretion from the pancreas. The second one is a group called insulin resistance-improving agents launched in recent years. These drugs decrease blood glucose levels by promoting sugar uptake in peripheral tissues without directly promoting insulin release. The third one is α-glucosidase inhibitors, which are drugs controlling a sharp rise in blood glucose level by delaying the digestion and absorption of carbohydrate in the gastrointestinal tract and suppressing a transient rise in blood glucose level after meals.

On the other hand, glucagon-like peptide-1 (hereinafter, referred to as GLP-1) is a hormone secreted by the stimulation of diets or the like from L cells, which are endocrine cells present in the epithelium of the small intestinal tract, and is known to decrease blood glucose levels by promoting insulin secretion through its action on β cells present in the pancreatic islets of Langerhans (Eur. J. Clin. Invest, Vol. 22, p. 154, 1992). The insulin secretory effect of GLP-1 depends on blood glucose levels. It has been reported that the insulin secretion mediated by GLP-1 is not observed in normal blood glucose and increased insulin secretion is seen only in hyperglycemia (Lancet, Vol. 2, p. 1300, 1987). Since GLP-1 not only increases insulin secretion but also

enhances the biosynthesis of insulin (Endocrinology, Vol. 130, p. 159, 1992) and promotes the growth of β cells (Diabetologia, Vol. 42, p. 856, 1999), it is also a factor indispensable to the maintenance of β cells.

The administration of GLP-1 to general patients with type II diabetes mellitus has been shown to significantly improve their hyperglycemic states as a result of keeping the GLP-1 concentration in blood at a high level, and its effectiveness for diabetes mellitus has also been confirmed in medical practice (Diabetologia, Vol. 36, p. 741, 1994; and Diabetologia, Vol. 39, p. 1546, 1996).

Furthermore, the active site of GLP-1 is not limited to β cells. GLP-1 has been confirmed to increase the utilization of sugars in peripheral tissues (Endocrinology, Vol. 135, p. 2070, 1994; and Diabetologia, Vol. 37, p. 1163, 1994). It has also been reported that GLP-1 exhibits antifeeding effect by intracerebroventricular administration (Digestion, Vol. 54, p. 360, 1993). It has further been reported that GLP-1 has inhibitory effect on gastrointestinal motility by administration (Dig. Dis. Sci., Vol. 43, p. 1113, 1998).

Compounds that are most structurally analogous to a compound of the present invention are described in JP 1994-505229 A (hereinafter, referred to as Reference A), JP 1994-507388 A (hereinafter, referred to as Reference B), JP 1994-510295 A (hereinafter, referred to as Reference C), U.S. Patent No. 3334113 (hereinafter, referred to as Reference D), U.S. Patent No. 3408350 (hereinafter, referred to as Reference E), U.S. Patent No. 3507863

(hereinafter, referred to as Reference F), British Patent No. 1038735 (hereinafter, referred to as Reference G), British Patent No. 1039117 (hereinafter, referred to as Reference H), U.S. Patent No. 3311629 (hereinafter, referred to as Reference I), U.S. Patent No. 3336306 (hereinafter, referred to as Reference J), British Patent No. 1059175 (hereinafter, referred to as Reference K), and JP 4-270284 A (hereinafter, referred to as Reference L).

References A to L disclose compounds having an oxazoloisoindole, imidazoisoindole, or thiazoloisoindole skeleton.

However, the compound of the present invention has an oxazoloisoindole, imidazoisoindole, or thiazoloisoindole skeleton common to the compounds of References A to L, but is a compound totally structurally different from the compounds of References A to L in that the compound of the present invention has an aryl group, a carbocyclic aromatic group, and a heteroaromatic group (R^8-R^7-R) in which two substituent groups are substituted in series in the substituent moiety at position 9 on the skeleton, specifically, for example, a functional group such as an N-methylcarbamoylmethoxyphenyl group (the compounds of References A to L are free from the substituent groups or the like).

Moreover, uses of References A to C are antiviral pharmaceuticals, and uses of References D to K are anti-inflammatory drugs, anticonvulsant drugs, analgesics, mydriatics, or antidepressants. These uses are totally irrelevant to the use of the present invention, although they are identical in terms of

industrial application field.

Furthermore, use of Reference L is heat- or pressure-sensitive color formers and is thus different in industrial application field from the present invention and totally irrelevant to the use of the present invention.

Examples of prior arts disclosing an invention related to the use of the present invention include U.S. Patent No. 3928597 (hereinafter, referred to as Reference M) and U.S. Patent No. 3936471 (hereinafter, referred to as Reference N). References M and N relate to an invention of a method for treating hyperglycemia, comprising orally or parenterally administering a 2,3-dihydroimidazoisoindolol compound having a lower alkyl group substituted in the imidazo moiety condensed to the isoindole skeleton, and an imidazolylphenyl phenyl ketone compound, and disclose a compound having an imidazoisoindole skeleton in the patent specifications.

However, the compound of the present invention has an imidazoisoindole skeleton common to the compounds of References M and N, but is a compound totally structurally different from the compounds of References M and N in that the compound of the present invention has an aryl group, a carbocyclic aromatic group, and a heteroaromatic group (R^8-R^7-R) in which two substituent groups are substituted in series in the substituent moiety at position 9 on the skeleton (the compounds of References M and N are free from the substituent groups or the like). In addition, the feature of the inventions of References M and N is antihyperglycemic effect

that is achieved by administering the 2,3-dihydroimidazoisoindolol compound and the imidazolylphenyl phenyl ketone compound, as described in, for example, lines 39 to 45 in the 4th box of the specification of Reference M. However, the patent specifications disclose the imidazoisoindole compound merely as a synthetic intermediate of the 2,3-dihydroimidazoisoindolol compound and the imidazolylphenyl phenyl ketone compound and do not disclose that this compound is useful as a therapeutic drug for diabetes mellitus or a preventive agent for chronic diabetic complications. Thus, their inventions are essentially different in spirit from the present invention.

Another example includes JP 49-45400 B (hereinafter, referred to as Reference O). Reference O relates to an invention of a method for producing an anorexiant, comprising orally or parenterally administering an imidazoisoindolol compound having a hydroxy group substituted in position 5 of the imidazoisoindole skeleton, and discloses a compound having an imidazoisoindole skeleton in the patent specification.

However, the compound of the present invention has an imidazoisoindole skeleton common to the compound of Reference O, but is a compound totally structurally different from the compound of Reference O in that the compound of the present invention has an aryl group, a carbocyclic aromatic group, and a heteroaromatic group (R^8-R^7-R) in which two substituent groups are substituted in series in the substituent moiety at position 9 on the skeleton (the compound of References O is free from the substituent groups or

the like). In addition, the feature of the invention of Reference O is anorexic effect that is achieved by administering the imidazoisoindolol compound. However, the patent specification discloses the imidazoisoindole compound merely as a synthetic intermediate of the imidazoisoindolol compound and does not disclose that this compound is useful as a therapeutic drug for diabetes mellitus or a preventive agent for chronic diabetic complications. Thus, its invention is essentially different in spirit from the present invention.

Currently, drugs such as sulfonylurea agents, insulin resistance-improving agents, and α-glucosidase inhibitors are often used clinically as therapeutic drugs for diabetes mellitus. However, these are less-than-sufficient drugs due to the problems listed below. Specifically, due to a slow manifestation of effect and a long duration of action, the action of the sulfonylurea agents is difficult to exhibit in perfect timing for hyperglycemia after meals. Furthermore, these agents decrease fasting blood glucose and may often cause life-threatening, serious hypoglycemic attack. The insulin resistance-improving agents often present the problem of adverse reaction to the liver and require careful use under strict control. Moreover, they may also cause adverse reaction such as edema. Alternatively, the α-glucosidase inhibitors have the problem of adverse reaction such as a feeling of fullness or diarrhea.

Thus, with recent increase in the number of diabetes mellitus patients, it is currently demanded from clinical practice to develop

a more beneficial therapeutic drug for diabetes mellitus that can control blood glucose levels in a blood glucose level-dependent manner without adverse reaction.

DISCLOSURE OF THE INVENTION

An object of the present invention is to provide a therapeutic agent for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug, or the like, because it exhibits an activity that achieves a high GLP-1 concentration in blood.

The present inventors have pursued diligent studies for the purpose of developing a therapeutic drug for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug that can control blood glucose levels in a blood glucose level-dependent manner. Consequently, the present inventors have completed the present invention by finding that a compound represented by the general formula [I] or [II] shown below achieves a high GLP-1 concentration in blood *in vivo*.

A compound represented by the general formula [I]:

wherein

R represents: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group,

an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; an aryl group which may have one or more substituent(s) selected from the group consisting of a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group, a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group

substituted by the heterocyclic group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C1-C_6 alkoxy group, a C_1-C_6 alkylthio group, and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; or a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group;

R^1 and R^2 are the same or different and each represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an aryl group,

an N-arylamino group, an aryloxy group, an arylsulfonyl group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an aroyl group, an N-aroylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an N-C_1-C_6 alkylamino group, or a C_1-C_6 alkoxy group which may be substituted by the substituent;

R^3, R^4, R^5, and R^6 each independently represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; a substituent selected from the group

consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, and a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the substituent; an aryl group which may have one or more substituent(s) selected from the group consisting of a substituent selected from the group consisting of an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, and an N-C_1-C_6 alkylamino group which may be

substituted by the substituent; a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, or a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the aryl group, the carbocyclic aromatic group, the heterocyclic group, or the heteroaromatic group, or R^3 and R^4 or R^5 and R^6 together form a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a 5- or 6-membered saturated carbocyclic group, a 5- or 6-membered unsaturated carbocyclic ring, or a 5- or 6-membered heterocyclic group, or R^3, R^4, R^5, and R^6 together form a condensed aryl group, a bicyclic or

tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group, or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom;

R^7 represents a hydrogen atom or a substituent selected from the group consisting of a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an aralkyl group, an aralkyloxy group, an aralkylcarbonyl group, an N-aralkylcarbamoyl group, an aryl group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, a C_2-C_6 alkanoyloxy group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group substituted by R^8, and a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl

group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group;

R^8 represents a substituent selected from the group consisting of a substituent selected from the group consisting of an azide group, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a sulfamoyl group, a sulfo group, a nitro group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, an N-aroylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_6 alkoxycarbonyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group,

an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group;

X represents an oxygen atom or a sulfur atom;

Y represents an oxygen atom, a group: $S=O_n$ (wherein n represents an integer of 0 to 2), or a group: NR^9 (wherein R^9 represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or C_1-C_6 alkylsulfonyl group which may be substituted by the substituent); and

Z represents: a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group selected from the group consisting of a condensed aryl group, a C_6-C_8 cycloalkanyl group, a C_6-C_8 cycloalkadienyl group, and a C_6-C_8 cycloalkenyl group; or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen

atom, and a sulfur atom, the bicyclic or tricyclic condensed heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group.

A compound represented by the general formula [II]:

wherein

R represents: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6

alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; an aryl group which may have one or more substituent(s) selected from the group consisting of a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group, a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C1-C_6 alkoxy group, a C_1-C_6 alkylthio group, and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; or a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a

pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group;

R^1 and R^2 are the same or different and each represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an aroyl group, an N-aroylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an N-C_1-C_6 alkylamino group, or a C_1-C_6 alkoxy group

which may be substituted by the substituent;

R^3, R^4, R^5, and R^6 each independently represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, and a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the substituent; an aryl group which may have one or more substituent(s) selected from the group consisting of a substituent selected from the group consisting of an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an aryloxy group, an

arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a

dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, or a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the aryl group, the carbocyclic aromatic group, the heterocyclic group, or the heteroaromatic group, or R^3 and R^4 or R^5 and R^6 together form a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a 5- or 6-membered saturated carbocyclic group, a 5- or 6-membered unsaturated carbocyclic ring, or a 5- or 6-membered heterocyclic group, or R^3, R^4, R^5, and R^6 together form a condensed aryl group, a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group, or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom;

R^7 represents a substituent selected from the group consisting of a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an aralkyl group, an aralkyloxy group, an aralkylcarbonyl group, an N-aralkylcarbamoyl group, an aryl group, an aryloxy group, an arylsulfonyl group, an

arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, a C_2-C_6 alkanoyloxy group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group substituted by R^8, and a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group;

R^8 represents a substituent selected from the group consisting of a substituent selected from the group consisting of an azide group, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a sulfamoyl group, a sulfo group, a nitro group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, an N-aroylamino group, a

C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_6 alkoxycarbonyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group;

X represents an oxygen atom or a sulfur atom;

Y represents an oxygen atom, a group: $S=O_n$ (wherein n represents an integer of 0 to 2), or a group: NR^9 (wherein R^9 represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group, a formyl group, a C_1-C_6 alkylsulfonyl

group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or C_1-C_6 alkylsulfonyl group which may be substituted by the substituent); and

Z represents: a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group selected from the group consisting of a condensed aryl group, a C_6-C_8 cycloalkanyl group, a C_6-C_8 cycloalkadienyl group, and a C_6-C_8 cycloalkenyl group; or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the bicyclic or tricyclic condensed heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group.

The present invention relates to an isoindole derivative and use thereof. These aspects of the present invention are a novel compound (compound represented by the general formula [II]) undescribed in documents and a known compound (compound represented by the general formula [I]) and have been totally unknown to be used for the purposes as described above as use thereof.

Next, the definitions of various symbols and terms described in the present specification will be described.

The aryl group is preferably an aryl group having 6 to 15 carbon atoms. Examples thereof include a naphthyl group and a phenyl group. Among them, for example, a phenyl group is preferable.

Examples of the 5- or 6-membered heterocyclic group include an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group. Among them, for example, a thienyl group, a tetrahydrofuranyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a furyl group, a dioxanyl group, and a morpholino group are preferable.

Examples of the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom include an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group. Among them, for example, an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, and a methylenedioxyphenyl group are preferable.

The halogen atom means, for example, a fluorine atom, a chlorine atom, a bromine atom, or an iodine atom. Among them, for

example, a fluorine atom, a chlorine atom, and an iodine atom are preferable, and, for example, a fluorine atom and a chlorine atom are more preferable.

The aralkyl group is preferably an aralkyl group having 7 to 15 carbon atoms. Specific examples thereof include a benzyl group, an α-methylbenzyl group, a phenethyl group, a 3-phenylpropyl group, a 1-naphthylmethyl group, a 2-naphthylmethyl group, an α-methyl(1-naphthyl)methyl group, an α-methyl(2-naphthyl)methyl group, an α-ethyl(1-naphthyl)methyl group, an α-ethyl(2-naphthyl)methyl group, a diphenylmethyl group, and a dinaphthylmethyl group. Particularly, for example, a benzyl group, a 1-naphthylmethyl group, a 2-naphthylmethyl group, an α-methylbenzyl group, and a phenethyl group are preferable.

The N-aralkylamino group means a group in which an amino group is substituted by the aralkyl group exemplified above. Specific examples thereof include an N-benzylamino group, an N-(α-methylbenzyl)amino group, an N-phenethylamino group, an N-(3-phenylpropyl)amino group, an N-(1-naphthylmethyl)amino group, an N-(2-naphthylmethyl)amino group, an N-[α-methyl(1-naphthyl)methyl]amino group, an N-[α-methyl(2-naphthyl)methyl]amino group, an N-[α-ethyl(1-naphthyl)methyl]amino group, an N-[α-ethyl(2-naphthyl)methyl]amino group, a diphenylmethylamino group, and an N-(dinaphthylmethyl)amino group. Particularly, for example, an N-benzylamino group, an N-(α-methylbenzyl)amino group,

and an N-phenethylamino group are preferable.

The aralkyloxy group means a group in which an oxygen atom is substituted by the aralkyl group exemplified above. Specific examples thereof include a benzyloxy group, an α-methylbenzyloxy group, a phenethyloxy group, a 3-phenylpropoxy group, a 1-naphthylmethoxy group, a 2-naphthylmethoxy group, an α-methyl(1-naphthyl)methoxy group, an α-methyl(2-naphthyl)methoxy group, an α-ethyl(1-naphthyl)methoxy group, an α-ethyl(2-naphthyl)methoxy group, a diphenylmethoxy group, and a dinaphthylmethoxy group. Particularly, for example, a benzyloxy group, an α-methylbenzyloxy group, and a phenethyloxy group are preferable.

The aralkylcarbonyl group means a group in which a carbonyl group is substituted by the aralkyl group exemplified above. Specific examples thereof include a benzylcarbonyl group, an α-methylbenzylcarbonyl group, a phenethylcarbonyl group, a 3-phenylpropylcarbonyl group, a 1-naphthylmethylcarbonyl group, a 2-naphthylmethylcarbonyl group, an α-methyl(1-naphthyl)methylcarbonyl group, an α-methyl(2-naphthyl)methylcarbonyl group, an α-ethyl(1-naphthyl)methylcarbonyl group, an α-ethyl(2-naphthyl)methylcarbonyl group, a diphenylmethylcarbonyl group, and a dinaphthylmethylcarbonyl group. Particularly, for example, a benzylcarbonyl group, an α-methylbenzylcarbonyl group, and a phenethylcarbonyl group are

preferable.

The N-aralkylcarbamoyl group means a group in which a carbamoyl group is substituted by the aralkyl group exemplified above. Specific examples thereof include an N-benzylcarbamoyl group, an N-(α-methylbenzyl)carbamoyl group, an N-phenethylcarbamoyl group, an N-(3-phenylpropyl)carbamoyl group, an N-(1-naphthylmethyl)carbamoyl group, an N-(2-naphthylmethyl)carbamoyl group, an N-(α-methyl(1-naphthyl)methyl)carbamoyl group, an N-(α-methyl(2-naphthyl)methyl)carbamoyl group, an N-(α-ethyl(1-naphthyl)methyl)carbamoyl group, an N-(α-ethyl(2-naphthyl)methyl)carbamoyl group, an N-(diphenylmethyl)carbamoyl group, and an N-(dinaphthylmethyl)carbamoyl group. Particularly, for example, an N-benzylcarbamoyl group, an N-(α-methylbenzyl)carbamoyl group, and an N-phenethylcarbamoyl group are preferable.

The N-arylamino group means a group in which an amino group is substituted by the aryl group exemplified above. Specific examples thereof include an N-phenylamino group, an N-(1-naphthyl)amino group, and an N-(2-naphthyl)amino group. Among them, for example, an N-phenylamino group is preferable.

The aryloxy group means a group in which an oxygen atom is substituted by the aryl group exemplified above. Specific examples thereof include a phenoxy group and a naphthyloxy group. Among them, for example, a phenoxy group is preferable.

The arylsulfonyl group means a group in which a sulfonyl group is substituted by the aryl group exemplified above. Specific examples thereof include a phenylsulfonyl group and a naphthylsulfonyl group. Among them, for example, a phenylsulfonyl group is preferable.

The N-arylcarbamoyl group means a group in which a carbamoyl group is substituted by the aryl group exemplified above. Specific examples thereof include an N-phenylcarbamoyl group and an N-naphthylcarbamoyl group. Among them, for example, an N-phenylcarbamoyl group is preferable.

The arylsulfamoyl group means a group in which a sulfamoyl group is substituted by the aryl group exemplified above. Specific examples thereof include a phenylsulfamoyl group and a naphthylsulfamoyl group. Among them, for example, a phenylsulfamoyl group is preferable.

The N-arylcarbamoyl group means a group in which a carbamoyl group is N-substituted by the aryl group exemplified above. Specific examples thereof include a phenylcarbamoyl group and a naphthylcarbamoyl group. Among them, for example, a phenylcarbamoyl group is preferable.

The C_2-C_6 alkanoyl group is preferably a group in which a carbonyl group is substituted by an alkyl group having 1 to 5 carbon atoms. Specific examples thereof include an acetyl group, a propionyl group, a butyryl group, an isobutyryl group, a valeryl group, an isovaleryl group, a pivaloyl group, and a pentanoyl group. Among them, for example, an acetyl group, a propionyl group, and

a pivaloyl group are preferable.

The N-C_2-C_6 alkanoylamino group means a group in which an amino group is substituted by the C_2-C_6 alkanoyl group exemplified above. Specific examples thereof include an N-acetylamino group, an N-propionylamino group, an N-butyrylamino group, an N-isobutyrylamino group, an N-valerylamino group, an N-isovalerylamino group, an N-pivaloylamino group, and an N-pentanoylamino group. Among them, for example, an N-acetylamino group, an N-propionylamino group, and an N-pivaloylamino group are preferable.

The C_2-C_6 alkanoyloxy group means a group in which an oxygen atom is substituted by the C_2-C_6 alkanoyl group exemplified above. Specific examples thereof include an acetoxy group, a propionyloxy group, a butyryloxy group, an isobutyryloxy group, a valeryloxy group, an isovaleryloxy group, a pivaloyloxy group, and a pentanoyloxy group. Among them, for example, an acetyloxy group, a propionyloxy group, and a pivaloyloxy group are preferable.

The aroyl group means a group in which a carbonyl group is substituted by the aryl group exemplified above. Specific examples thereof include a benzoyl group and a naphthylcarbonyl group. Among them, for example, a benzoyl group is preferable.

The aroxy group means a group in which an oxygen atom is substituted by the aroyl group exemplified above. Specific examples thereof include a benzoyloxy group and a naphthylcarbonyloxy group. Among them, for example, a benzoyloxy group is preferable.

The N-aroylamino group means a group in which an amino group is N-substituted by the aroyl group exemplified above. Specific examples thereof include an N-benzoylamino group and an N-naphthylcarbonylamino group. Among them, for example, an N-benzoylamino group is preferable.

The N-C_1-C_6 alkylamino group is preferably a group in which an amino group is N-substituted by an alkyl group having 1 to 6 carbon atoms. Specific examples thereof include an N-methylamino group, an N-ethylamino group, an N-propylamino group, an N-isopropylamino group, an N-butylamino group, an N-isobutylamino group, an N-sec-butylamino group, an N-tert-butylamino group, an N-pentylamino group, an N-neopentylamino group, an N-hexylamino group, and an N-isohexylamino group. Among them, for example, an N-methylamino group, an N-ethylamino group, an N-propylamino group, an N-isopropylamino group, an N-butylamino group, an N-isobutylamino group, and an N-tert-butylamino group are preferable.

The N,N-di-C_1-C_6 alkylamino group is preferably a group in which an amino group is N,N-di-substituted by an alkyl group having 1 to 6 carbon atoms. Specific examples thereof include an N,N-dimethylamino group, an N,N-diethylamino group, an N,N-dipropylamino group, an N,N-diisopropylamino group, an N,N-dibutylamino group, an N,N-di-tert-butylamino group, an N,N-dipentylamino group, an N,N-dihexylamino group, an N-ethyl-N-methylamino group, an N-methyl-N-propylamino group, an N-isopropyl-N-methylamino group, an N-tert-butyl-N-methylamino

group, and an N-ethyl-N-isopropylamino group. Among them, for example, an N,N-dimethylamino group, an N,N-diethylamino group, an N,N-diisopropylamino group, an N,N-dibutylamino group, an N,N-di-tert-butylamino group, an N-ethyl-N-methylamino group, an N-methyl-N-propylamino group, an N-isopropyl-N-methylamino group, and an N-ethyl-N-isopropylamino group are preferable.

The N-C_1-C_{10} alkylcarbamoyl group is preferably a group in which a carbamoyl group is N-substituted by an alkyl group having 1 to 10 carbon atoms. Specific examples thereof include an N-methylcarbamoyl group, an N-ethylcarbamoyl group, an N-propylcarbamoyl group, an N-isopropylcarbamoyl group, an N-butylcarbamoyl group, an N-isobutylcarbamoyl group, an N-sec-butylcarbamoyl group, an N-tert-butylcarbamoyl group, an N-pentylcarbamoyl group, an N-neopentylcarbamoyl group, an N-hexylcarbamoyl group, an N-isohexylcarbamoyl group, an N-octylcarbamoyl group, and an N-decylcarbamoyl group. Among them, for example, an N-methylcarbamoyl group, an N-ethylcarbamoyl group, an N-propylcarbamoyl group, an N-isopropylcarbamoyl group, an N-isobutylcarbamoyl group, an N-sec-butylcarbamoyl group, an N-tert-butylcarbamoyl group, an N-octylcarbamoyl group, and an N-decylcarbamoyl group are preferable.

The N,N-di-C_1-C_{10} alkylcarbamoyl group is preferably a group in which a carbamoyl group is N,N-di-substituted by an alkyl group having 1 to 10 carbon atoms. Specific examples thereof include an N,N-dimethylcarbamoyl group, an N,N-diethylcarbamoyl group, an N,N-dipropylcarbamoyl group, an N,N-diisopropylcarbamoyl group,

an N,N-dibutylcarbamoyl group, an N,N-di-tert-butylcarbamoyl group, an N,N-dipentylcarbamoyl group, an N,N-dihexylcarbamoyl group, an N-ethyl-N-methylcarbamoyl group, an N-isopropyl-N-methylcarbamoyl group, an N-tert-butyl-N-methylcarbamoyl group, and an N-ethyl-N-isopropylcarbamoyl group. Among them, for example, an N,N-dimethylcarbamoyl group, an N,N-diethylcarbamoyl group, an N,N-diisopropylcarbamoyl group, an N,N-dibutylcarbamoyl group, an N,N-di-tert-butylcarbamoyl group, an N-ethyl-N-methylcarbamoyl group, an N-isopropyl-N-methylcarbamoyl group, and an N-ethyl-N-isopropylcarbamoyl group are preferable.

The N-C_1-C_{10} alkylthiocarbamoyl group is preferably a group in which a thiocarbamoyl group is N-substituted by an alkyl group having 1 to 10 carbon atoms. Specific examples thereof include an N-methylthiocarbamoyl group, an N-ethylthiocarbamoyl group, an N-propylthiocarbamoyl group, an N-isopropylthiocarbamoyl group, an N-butylthiocarbamoyl group, an N-isobutylthiocarbamoyl group, an N-sec-butylthiocarbamoyl group, an N-tert-butylthiocarbamoyl group, an N-pentylthiocarbamoyl group, an N-neopentylthiocarbamoyl group, an N-hexylthiocarbamoyl group, an N-isohexylthiocarbamoyl group, an N-octylthiocarbamoyl group, and an N-decylthiocarbamoyl group. Among them, for example, an N-methylthiocarbamoyl group, an N-ethylthiocarbamoyl group, an N-propylthiocarbamoyl group, an N-isopropylthiocarbamoyl group, an N-isobutylthiocarbamoyl group, an N-sec-butylthiocarbamoyl group, an N-tert-butylthiocarbamoyl group, an

N-octylthiocarbamoyl group, and an N-decylthiocarbamoyl group are preferable.

The N-amino-C_1-C_{10} alkylcarbamoyl group is preferably a group in which a carbamoyl group is substituted by an aminoalkyl group having 1 to 10 carbon atoms. Specific examples thereof include an N-aminomethylcarbamoyl group, an N-aminoethylcarbamoyl group, an N-aminopropylcarbamoyl group, an N-aminomethylethylcarbamoyl group, an N-aminobutylcarbamoyl group, an N-aminopropylcarbamoyl group, an N-aminopentylcarbamoyl group, and an N-aminohexylcarbamoyl group. Among them, for example, an N-aminomethylcarbamoyl group, an N-aminoethylcarbamoyl group, an N-aminopropylcarbamoyl group, and an N-aminomethylethylcarbamoyl group are preferable.

The N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group is preferably a group in which the C_1-C_{10} alkylcarbamoyl group exemplified above is N-substituted by an alkoxy group having 1 to 6 carbon atoms. Specific examples thereof include an N-methoxymethylcarbamoyl group, an N-methoxyethylcarbamoyl group, an N-methoxypropylcarbamoyl group, an N-methoxybutylcarbamoyl group, an N-ethoxypentylcarbamoyl group, and an N-butoxyhexylcarbamoyl group. Among them, for example, an N-methoxymethylcarbamoyl group, an N-methoxyethylcarbamoyl group, an N-methoxypropylcarbamoyl group, and an N-methoxybutylcarbamoyl group are preferable.

The N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group is preferably a group in which the C_1-C_{10} alkylcarbamoyl group exemplified above is N-substituted by an alkoxycarbonyl group

having 1 to 6 carbon atoms. Specific examples thereof include an N-methoxycarbonylmethylcarbamoyl group, an N-methoxycarbonylethylcarbamoyl group, an N-methoxycarbonylpropylcarbamoyl group, an N-methoxycarbonylbutylcarbamoyl group, an N-ethoxycarbonylpentylcarbamoyl group, an N-butoxycarbonylhexylcarbamoyl group, and an N-tert-butoxycarbonylethylcarbamoyl group. Among them, for example, an N-methoxycarbonylmethylcarbamoyl group, an N-methoxycarbonylethylcarbamoyl group, an N-methoxycarbonylpropylcarbamoyl group, an N-methoxycarbonylbutylcarbamoyl group, and an N-tert-butoxycarbonylethylcarbamoyl group are preferable.

The N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group is preferably a group in which a C_1-C_{10} alkylcarbamoyl group is N-substituted by an alkoxycarbonylamino group having 1 to 6 carbon atoms. Specific examples thereof include an N-methoxycarbonylaminomethylcarbamoyl group, an N-methoxycarbonylaminoethylcarbamoyl group, an N-methoxycarbonylaminopropylcarbamoyl group, an N-methoxycarbonylaminobutylcarbamoyl group, an N-ethoxycarbonylaminopentylcarbamoyl group, an N-butoxycarbonylaminohexylcarbamoyl group, and an N-tert-butoxycarbonylaminoethylcarbamoyl group. Among them, for example, an N-methoxycarbonylaminomethylcarbamoyl group, an N-methoxycarbonylaminoethylcarbamoyl group, an

N-methoxycarbonylaminopropylcarbamoyl group, an N-methoxycarbonylaminobutylcarbamoyl group, and an N-tert-butoxycarbonylaminoethylcarbamoyl group are preferable.

The N-C_1-C_6 alkoxycarbonylamino-C_1-C_6 alkoxycarbonyl group is preferably a group in which a C_1-C_6 alkoxycarbonyl group is N-substituted by an alkoxycarbonylamino group having 1 to 6 carbon atoms. Specific examples thereof include an N-methoxycarbonylaminomethoxycarbonyl group, an N-methoxycarbonylaminoethoxycarbonyl group, an N-methoxycarbonylaminopropoxycarbonyl group, an N-methoxycarbonylaminobutoxycarbonyl group, an N-ethoxycarbonylaminopentyloxycarbonyl group, an N-butoxycarbonylaminohexyloxycarbonyl group, and an N-tert-butoxycarbonylaminoethoxycarbonyl group. Among them, for example, an N-methoxycarbonylaminomethoxycarbonyl group, an N-methoxycarbonylaminoethoxycarbonyl group, an N-methoxycarbonylaminopropoxycarbonyl group, an N-methoxycarbonylaminobutoxycarbonyl group, and an N-tert-butoxycarbonylaminoethoxycarbonyl group are preferable.

The N-C_2-C_6 alkenylcarbamoyl group is preferably a group in which a carbamoyl group is N-substituted by an alkenyl group having 2 to 6 carbon atoms. Specific examples thereof include an N-vinylcarbamoyl group, an N-allylcarbamoyl group, an N-(1-propenyl)carbamoyl group, an N-isopropenylcarbamoyl group, an N-(2-butenyl)carbamoyl group, an N-isobutenylcarbamoyl group, an N-(2-pentenyl)carbamoyl group, an N-(2-hexenyl)carbamoyl group,

an N-(2-heptenyl)carbamoyl group, and an N-(2-octenyl)carbamoyl group. Among them, for example, an N-vinylcarbamoyl group, an N-allylcarbamoyl group, and an N-(1-propenyl)carbamoyl group are preferable.

The N-C_1-C_6 alkylsulfamoyl group is preferably a group in which a sulfamoyl group is N-substituted by an alkyl group having 1 to 6 carbon atoms. Specific examples thereof include an N-methylsulfamoyl group, an N-ethylsulfamoyl group, an N-propylsulfamoyl group, an N-isopropylsulfamoyl group, an N-butylsulfamoyl group, an N-isobutylsulfamoyl group, an N-sec-butylsulfamoyl group, an N-tert-butylsulfamoyl group, an N-pentylsulfamoyl group, an N-neopentylsulfamoyl group, an N-hexylsulfamoyl group, and an N-isohexylsulfamoyl group. Among them, for example, N-methylsulfamoyl group, an N-ethylsulfamoyl group, an N-isopropylsulfamoyl group, and an N-tert-butylsulfamoyl group are preferable.

The C_1-C_6 alkylsulfinyl group is preferably a group in which a sulfinyl group is substituted by an alkyl group having 1 to 6 carbon atoms. Specific examples thereof include a methylsulfinyl group, an ethylsulfinyl group, a propylsulfinyl group, an isopropylsulfinyl group, a butylsulfinyl group, an isobutylsulfinyl group, a sec-butylsulfinyl group, a tert-butylsulfinyl group, a pentylsulfinyl group, a neopentylsulfinyl group, a hexylsulfinyl group, and an isohexylsulfinyl group. Among them, for example, a methylsulfinyl group, an ethylsulfinyl group, a propylsulfinyl group, an

isopropylsulfinyl group, a butylsulfinyl group, and a tert-butylsulfinyl group are preferable.

The C_1-C_6 alkylsulfonyl group is preferably a group in which a sulfonyl group is substituted by an alkyl group having 1 to 6 carbon atoms. Specific examples thereof include a methylsulfonyl group, an ethylsulfonyl group, a propylsulfonyl group, an isopropylsulfonyl group, a butylsulfonyl group, an isobutylsulfonyl group, a sec-butylsulfonyl group, a tert-butylsulfonyl group, a pentylsulfonyl group, a neopentylsulfonyl group, a hexylsulfonyl group, and an isohexylsulfonyl group. Among them, for example, a methylsulfonyl group, an ethylsulfonyl group, a propylsulfonyl group, a butylsulfonyl group, and a tert-butylsulfonyl group are preferable.

The N-C_1-C_6 alkylsulfonylamino group is preferably a group in which a sulfonylamino group is substituted by an alkyl group having 1 to 6 carbon atoms. Specific examples thereof include an N-methylsulfonylamino group, an N-ethylsulfonylamino group, an N-propylsulfonylamino group, an N-isopropylsulfonylamino group, an N-butylsulfonylamino group, an N-isobutylsulfonylamino group, an N-sec-butylsulfonylamino group, an N-tert-butylsulfonylamino group, an N-pentylsulfonylamino group, an N-neopentylsulfonylamino group, an N-hexylsulfonylamino group, and an N-isohexylsulfonylamino group. Among them, for example, an N-methylsulfonylamino group, an N-ethylsulfonylamino group, an N-propylsulfonylamino group, an N-butylsulfonylamino group, and an N-tert-butylsulfonylamino group are preferable.

The C_1-C_6 alkylthio group is preferably a group in which a sulfur atom is substituted by an alkyl group having 1 to 6 carbon atoms. Specific examples thereof include a methylthio group, an ethylthio group, a propylthio group, an isopropylthio group, a butylthio group, an isobutylthio group, a sec-butylthio group, a tert-butylthio group, a pentylthio group, a neopentylthio group, a hexylthio group, and an isohexylthio group. Among them, for example, a methylthio group, an ethylthio group, a propylthio group, an isopropylthio group, a butylthio group, and a tert-butylthio group are preferable.

The C_1-C_6 alkoxy group is preferably a group in which an oxygen atom is substituted by an alkyl group having 1 to 6 carbon atoms. Specific examples thereof include a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group, a pentyloxy group, a neopentyloxy group, a hexyloxy group, and an isohexyloxy group. Among them, for example, a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, an isobutoxy group, and a tert-butoxy group are preferable.

The C_1-C_6 alkoxycarbonyl group is preferably a group in which a carbonyl group is substituted by an alkoxy group having 1 to 5 carbon atoms. Specific examples thereof include a methoxycarbonyl group, an ethoxycarbonyl group, a propoxycarbonyl group, an isopropoxycarbonyl group, a butoxycarbonyl group, an isobutoxycarbonyl group, a sec-butoxycarbonyl group, a tert-butoxycarbonyl group, a pentyloxycarbonyl group, and a

neopentyloxycarbonyl group. Among them, for example, a methoxycarbonyl group, an ethoxycarbonyl group, a propoxycarbonyl group, an isopropoxycarbonyl group, a butoxycarbonyl group, and a tert-butoxycarbonyl group are preferable.

The N-C_3-C_6 cycloalkylamino group is preferably a group in which an amino group is N-substituted by a cyclic alkyl group having 3 to 6 carbon atoms. Examples thereof include an N-cyclopropylamino group, an N-cyclobutylamino group, an N-cyclopentylamino group, and an N-cyclohexylamino group. Among them, for example, an N-cyclopropylamino group, an N-cyclopentylamino group, and an N-cyclohexylamino group are preferable.

The C_3-C_6 cycloalkyloxy group is preferably a group in which an oxygen atom is substituted by a cyclic alkyl group having 3 to 6 carbon atoms. Examples thereof include an N-cyclopropoxy group, an N-cyclobutoxy group, an N-cyclopentyloxy group, and an N-cyclohexyloxy. Among them, for example, an N-cyclopropoxy group, an N-cyclopentyloxy group, and an N-cyclohexyloxy group are preferable.

The N-C_3-C_6 cycloalkylcarbamoyl group is preferably a group in which a carbamoyl group is N-substituted by a cyclic alkyl group having 3 to 6 carbon atoms. Examples thereof include an N-cyclopropylcarbamoyl group, an N-cyclobutylcarbamoyl group, an N-cyclopentylcarbamoyl group, and an N-cyclohexylcarbamoyl group. Among them, for example, an N-cyclopropylcarbamoyl group, an N-cyclopentylcarbamoyl group, and an N-cyclohexylcarbamoyl group

are preferable.

The saturated C_1-C_9 aliphatic group is preferably an alkyl group having 1 to 9 carbon atoms and may be linear or branched. Among them, a linear or branched alkyl group having 1 to 6 carbon atoms is preferable.

Examples of the alkyl group include a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, a neopentyl group, a hexyl group, an isohexyl group, a heptyl group, an octyl group, and a nonyl group. Among them, for example, a methyl group, an ethyl group, a propyl group, an isopropyl group, an isobutyl group, a sec-butyl group, and a tert-butyl group are preferable.

The unsaturated C_1-C_9 aliphatic group is preferably an alkenyl group or alkynyl group having 1 to 9 carbon atoms and may be linear or branched. Among them, a linear or branched alkenyl group or alkynyl group having 1 to 6 carbon atoms is preferable.

Examples of the alkenyl group include a vinyl group, an allyl group, a 1-propenyl group, an isopropenyl group, a 2-butenyl group, an isobutenyl group, a 2-pentenyl group, a 2-hexenyl group, a 2-heptenyl group, and a 2-octenyl group. Among them, for example, a vinyl group, an allyl group, and a 1-propenyl group are preferable.

Examples of the alkynyl group include an ethynyl group, a 1-propynyl group, a 1-butenyl group, a 1-pentenyl group, a 1-hexynyl group, a 1-heptynyl group, and a 1-octynyl group. Among them, for example, an ethynyl group and a 1-propynyl group are preferable.

Examples of the 5- or 6-membered saturated carbocyclic group include a cyclopentyl group and a cyclohexyl group. Among them, for example, a cyclopentyl group is preferable.

Examples of the 5- or 6-membered unsaturated carbocyclic group include a cyclopentenyl group and a cyclohexenyl group. Among them, for example, a cyclopentenyl group is preferable.

The N-C_1-C_{10} alkylcarbamoyl group or the N-C_1-C_{10} alkylthiocarbamoyl group substituted by the 5- or 6-membered heterocyclic group is preferably an N-C_1-C_{10} alkylcarbamoyl group or an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group exemplified above. Specific examples thereof include: an N-imidazolylalkylcarbamoyl group such as an N-imidazolylmethylcarbamoyl group, an N-oxazolylalkylcarbamoyl group such as an N-oxazolylmethylcarbamoyl group, an N-thiazolylalkylcarbamoyl group such as an N-thiazolylmethylcarbamoyl group, an N-thiadiazolylalkylcarbamoyl group such as an N-thiadiazolylmethylcarbamoyl group, an N-thienylalkylcarbamoyl group such as an N-thienylmethylcarbamoyl group, an N-triazolylalkylcarbamoyl group such as an N-triazolylmethylcarbamoyl group, an N-pyridylalkylcarbamoyl group such as an N-pyridylmethylcarbamoyl group, an N-pyrazylalkylcarbamoyl group such as an N-pyrazylmethylcarbamoyl group, an N-pyrazinylalkylcarbamoyl group such as an N-pyrazinylmethylcarbamoyl group, an N-pyrimidinylalkylcarbamoyl group such as an N-pyrimidinylmethylcarbamoyl group, an

N-pyridazinylalkylcarbamoyl group such as an N-pyridazinylmethylcarbamoyl group, an N-pyrazolylalkylcarbamoyl group such as an N-pyrazolylmethylcarbamoyl group, an N-furylalkylcarbamoyl group such as an N-furylmethylcarbamoyl group, an N-tetrahydrofuranylalkylcarbamoyl group such as an N-tetrahydrofuranylmethylcarbamoyl group, an N-pyrrolidinylalkylcarbamoyl group such as an N-pyrrolidinylmethylcarbamoyl group, and an N-morpholinoalkylcarbamoyl group such as an N-morpholinomethylcarbamoyl group; and an N-imidazolylalkylthiocarbamoyl group such as an N-imidazolylmethylthiocarbamoyl group, an N-oxazolylalkylthiocarbamoyl group such as an N-oxazolylmethylthiocarbamoyl group, an N-thiazolylalkylthiocarbamoyl group such as an N-thiazolylmethylthiocarbamoyl group, an N-thiadiazolylalkylthiocarbamoyl group such as an N-thiadiazolylmethylthiocarbamoyl group, an N-thienylalkylthiocarbamoyl group such as an N-thienylmethylthiocarbamoyl group, an N-triazolylalkylthiocarbamoyl group such as an N-triazolylmethylthiocarbamoyl group, an N-pyridylalkylthiocarbamoyl group such as an N-pyridylmethylthiocarbamoyl group, an N-pyrazylalkylthiocarbamoyl group such as an N-pyrazylmethylthiocarbamoyl group, an

N-pyrazinylalkylthiocarbamoyl group such as an N-pyrazinylmethylthiocarbamoyl group, an N-pyrimidinylalkylthiocarbamoyl group such as an N-pyrimidinylmethylthiocarbamoyl group, an N-pyridazinylalkylthiocarbamoyl group such as an N-pyridazinylmethylthiocarbamoyl group, an N-pyrazolylalkylthiocarbamoyl group such as an N-pyrazolylmethylthiocarbamoyl group, an N-furylalkylthiocarbamoyl group such as an N-furylmethylthiocarbamoyl group, an N-tetrahydrofuranylalkylthiocarbamoyl group such as an N-tetrahydrofuranylmethylthiocarbamoyl group, an N-pyrrolidinyl alkylthiocarbamoyl group such as an N-pyrrolidinylmethylthiocarbamoyl group, and an N-morpholino alkylthiocarbamoyl group such as an N-morpholinomethylthiocarbamoyl group. Among them, for example, an N-C_1-C_{10} alkylcarbamoyl group or an N-C_1-C_{10} alkylthiocarbamoyl group substituted by a thienyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a furyl group, a tetrahydrofuranyl group, a morpholino group, or the like is preferable.

The condensed aryl group refers to a group in which, for example, a phenyl group or a naphthyl group is bound to another ring to form a condensed benzene ring or a condensed naphthalene ring.

Specific examples of the bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group include a C_6-C_8

cycloalkanyl group, a C_6-C_8 cycloalkadienyl group, and a C_6-C_8 cycloalkenyl group. Among them, for example, a C_6-C_8 cycloalkanyl group, a C_6-C_8 cycloalkadienyl group, and a C_6-C_8 cycloalkenyl group are preferable.

Examples of the C_6-C_8 cycloalkanyl group include a cyclohexanyl group, a cycloheptanyl group, and a cyclooctanyl group. Among them, for example, a cyclohexanyl group is preferable.

Examples of the C_6-C_8 cycloalkadienyl group include a cyclohexadienyl group, a cycloheptadienyl group, and a cyclooctadienyl group. Among them, for example, a cyclohexadienyl group is preferable.

Examples of the C_6-C_8 cycloalkenyl group include a cyclohexenyl group, a cycloheptenyl group, and a cyclooctenyl group. Among them, for example, a cyclohexenyl group is preferable.

Examples of the bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom include an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group. Among them, for example, an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, or a methylenedioxyphenyl group is preferable.

Next, the compound of the general formula [I] of the present

invention will be described.

Among the compounds represented by the general formula [I]:

[wherein R, R^1, R^2, R^3, R^4, R^5, R^6, R^7, X, Y, and Z are as defined above],

a preferable compound is a compound represented by the general formula [I-a] or a pharmaceutically acceptable salt thereof:

wherein R^a represents: a substituent selected from the group consisting of an amino group, a halogen atom, a hydroxy group, a C_1-C_6 alkylthio group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, and a C_1-C_6 alkoxy group; an aryl group which may have one or more substituent(s) selected from the group consisting of a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, a C_1-C_6 alkylthio group,

and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; or a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group; R^{1a} and R^{2a} are the same or different and each represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an aroyl group, an N-aroylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6

alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an N-C_1-C_6 alkylamino group, or a C_1-C_6 alkoxy group which may be substituted by the substituent; R^{3a}, R^{4a}, R^{5a}, and R^{6a} each independently represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, and a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the substituent; an aryl group which may have one or more substituent(s) selected from the group

consisting of a substituent selected from the group consisting of an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; a monocyclic to tricyclic heteroaromatic group having 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a

pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, or a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the aryl group, the carbocyclic aromatic group, the heterocyclic group, or the heteroaromatic group, or R^{3a} and R^{4a} or R^{5a} and R^{6a} together form a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, or a branched unsaturated C_1-C_9 aliphatic group, a 5- or 6-membered saturated carbocyclic group, a 5- or 6-membered unsaturated carbocyclic group, or a 5- or 6-membered heterocyclic group, or R^{3a}, R^{4a}, R^{5a}, and R^{6a} together form a condensed aryl group, a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group, or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom; R^{7a} represents

a hydrogen atom; X_a represents an oxygen atom or a sulfur atom; Y_a represents an oxygen atom, a group: $S{=}O_n$ (wherein n represents an integer of 0 to 2), or a group: NR^{9a} (wherein R^{9a} represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent); and Z_a represents: a condensed aryl group; a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group selected from the group consisting of a C_6-C_8 cycloalkanyl group, a C_6-C_8 cycloalkadienyl group, and a C_6-C_8 cycloalkenyl group; or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the bicyclic or tricyclic condensed heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group.

Next, the compound of the general formula [II] of the present invention will be described.

Among the compounds represented by the general formula [II]:

[wherein R, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, X, Y, and Z are as defined above],

a preferable compound is a compound represented by the general formula [II-b] or a pharmaceutically acceptable salt thereof:

wherein R^b represents: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6

alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; an aryl group which may have one or more substituent(s) selected from the group consisting of a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, a C_1-C_6 alkylthio group, and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; or a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting

of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group; R^{1b} and R^{2b} are the same or different and each represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an aroyl group, an N-aroylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an N-C_1-C_6 alkylamino group, or a C_1-C_6 alkoxy group which may be substituted by the substituent; R^{3b}, R^{4b}, R^{5b}, and R^{6b} each independently represent: a substituent selected from the group

consisting of a hydrogen atom, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, and a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the substituent; an aryl group which may have one or more substituent(s) selected from the group consisting of a substituent selected from the group consisting of an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an

N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group; or a linear

saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, or a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the aryl group, the carbocyclic aromatic group, the heterocyclic group, or the heteroaromatic group, or R^{3b} and R^{4b} or R^{5b} and R^{6b} together form a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a 5- or 6-membered saturated carbocyclic group, a 5- or 6-membered unsaturated carbocyclic group, or a 5- or 6-membered heterocyclic group, or R^{3b}, R^{4b}, R^{5b}, and R^{6b} together form a condensed aryl group, a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group, or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom; R^{7b} represents a substituent selected from the group consisting of a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an aralkyl group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, a C_2-C_6 alkanoyloxy group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10}

alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group substituted by R^{8b}, and a 5- or 6-membered heterocyclic group selected from the group consisting of a pyridyl group, a pyrazinyl group, a tetrahydrofuranyl group, a dioxanyl group, and a morpholino group; $R8^b$ represents a substituent selected from the group consisting of a substituent selected from the group consisting of an azide group, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a sulfamoyl group, a sulfo group, a nitro group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, an N-aroylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6

alkoxycarbonylamino-C_1-C_6 alkoxycarbonyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a furyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group; X_b represents an oxygen atom or a sulfur atom; Y_b represents an oxygen atom, a group: $S=O_n$, (wherein n represents an integer of 0 to 2), or a group: NR^{9b} (wherein R^{9b} represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent); and Z_b represents: a condensed aryl group; a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group selected from the group consisting of

a C_6-C_8 cycloalkanyl group, a C_6-C_8 cycloalkadienyl group, and a C_6-C_8 cycloalkenyl group; or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the bicyclic or tricyclic condensed heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group. More preferable is a compound represented by the general formula [II-c] or a pharmaceutically acceptable salt thereof:

wherein R^c represents: a substituent selected from the group consisting of an amino group, a carbamoyl group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a formylamino group, an aralkyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a

C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkoxycarbonyl group; an aryl group which may have one or more substituent(s) selected from the group consisting of a 5- or 6-membered heterocyclic group selected from the group consisting of a pyridyl group, a pyrazinyl group, a tetrahydrofuranyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group substituted by the heterocyclic group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkylthio group which may be substituted by the substituent; or a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of a pyridyl group, a pyrazinyl group, a tetrahydrofuranyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring being selected from the group consisting of an ethylenedioxyphenyl group and a methylenedioxyphenyl group; R^{1c} and R^{2c} are the same or different and each represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a

hydroxy group, a formyl group, a formylamino group, an N-C_1-C_6 alkylamino group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkoxycarbonyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or an N-C_1-C_6 alkylamino group which may be substituted by the substituent; R^{3c}, R^{4c}, R^{5c}, and R^{6c} each independently represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkoxycarbonyl group; a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, and a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the substituent; an aryl group which may have one or more substituent(s) selected from the group consisting of a substituent selected from the group consisting of an amino group, a carbamoyl group, a carboxyl group, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group, a formyl group, an N-C_1-C_6 alkylamino group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkoxycarbonyl group; a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of a pyridyl group, a pyrazinyl group, a tetrahydrofuranyl group,

a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring being selected from the group consisting of an ethylenedioxyphenyl group and a methylenedioxyphenyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, or a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the aryl group, the carbocyclic aromatic group, the heterocyclic group, or the heteroaromatic group, or R^{3c} and R^{4c} or R^{5c} and R^{6c} together form a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a 5- or 6-membered heterocyclic group, or R^{3c}, R^{4c}, R^{5c}, and R^{6c} together form a condensed aryl group; R^{7c} represents a substituent selected from the group consisting of a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an aryl group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, a C_2-C_6 alkanoyloxy group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6

alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkoxycarbonyl group substituted by R^{8c}; R^{8c} represents f a substituent selected from the group consisting of a substituent selected from the group consisting of an azide group, an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a sulfamoyl group, a sulfo group, a nitro group, a formyl group, a formylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_6 alkoxycarbonyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, a 5- or 6-membered heterocyclic group selected from the group consisting of a pyridyl group, a pyrazinyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group substituted by the heterocyclic group; X_c represents an oxygen atom or a sulfur atom; Y_c represents an oxygen atom, a group: $S=O_n$ (wherein n represents an integer of 0 to 2),

or a group: NR^{9c} (wherein R^{9c} represents a substituent selected from the group consisting of a hydrogen atom, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent); and Z_c represents a condensed aryl group or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the bicyclic or tricyclic condensed heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group.

Most preferable is a compound represented by the general formula [II-d] or a pharmaceutically acceptable salt thereof:

wherein R^d represents: an aryl group which may have one or more substituent(s) selected from the group consisting of an amino group, a carbamoyl group, a cyano group, a sulfamoyl group, a halogen atom, a hydroxy group, a formylamino group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an

N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkoxycarbonyl group; or a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of a pyridyl group, a pyrazinyl group, a tetrahydrofuranyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring being selected from the group consisting of an ethylenedioxyphenyl group and a methylenedioxyphenyl group; R^{1d} and R^{2d} are the same or different and each represent a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a cyano group, a sulfamoyl group, a halogen atom, a hydroxy group, a formylamino group, an N-C_1-C_6 alkylamino group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkoxycarbonyl group; R^{3d}, R^{4d}, R^{5d}, and R^{6d} each independently represent: a substituent selected from the group consisting of a hydrogen atom, an amino group, a carbamoyl group, a carboxyl group, a cyano group, a sulfamoyl group, a halogen atom, a hydroxy group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, and a C_1-C_6

alkoxycarbonyl group; or a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, and a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the substituent, or R^{3d} and R^{4d} or R^{5d} and R^{6d} together form a linear unsaturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a 5- or 6-membered heterocyclic group; R^{7d} represents a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, a C_1-C_6 alkylthio group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, and a C_1-C_6 alkoxycarbonyl group substituted by R^{8d}; R^{8d} represents a substituent selected from the group consisting of an amino group, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group, a sulfamoyl group, a formylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxy-C_1-C_{10}

alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group; X_d represents an oxygen atom or a sulfur atom; Y_d represents an oxygen atom, a group: $S=O_n$ (wherein n represents an integer of 0 to 2), or a group: NR^{9d} (wherein R^{9d} represents a substituent selected from the group consisting of a hydrogen atom, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent); and Z_d represents a condensed aryl group or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the bicyclic or tricyclic condensed heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, and a methylenedioxyphenyl group.

Typical examples of the compound represented by the general formula [I] according to the present invention:

[wherein R, R^1, R^2, R^3, R^4, R^5, R^6, R^7, X, Y, and Z are as defined above] (among them, those in which R^7 is a hydrogen atom) and the compound represented by the general formula [II] according to the present invention:

[wherein R, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, X, Y, and Z are as defined above]

are shown in Tables 1 to 44.

Of these compounds, preferable compounds are, for example, compounds of compound Nos. 1001 to 1024, 1028, 1034 to 1043, 1045, 1062, 1065, 1093, 1094, 1095, 1104, 1108, 1110, 1115, 1116, 1117, 1118, 1130, 1131, 1132, 1133, 1134, 1135, 1143, 1147, 1157, 1158, 1159, 1160, 1161, 1162, 1166, 1167, 2018, 2025, 2026, 2027, 2028, 2047, 2048, 2049, 2050, 2051, 2068, 2071, 2160, 2178, 2180, 2181, 2182, 2183, 3001, 3014, 3025, 3026, 3027, 3028, 3029, 3030, 3031, 3032, 3033, 3036, 3038, 3039, 3046, 3047, 3054, 3057, 3058, 3061, 3062, 3063, 3064, 3067, 3068, 3071, 3072, 3075, 3076, 3087, 3088, 3089, 3090, 3091, 3133, 3156, 3158, 3161, 3167, 3175, 3179, and 3182. Among them, for example, compounds of compound Nos. 1045, 1062, 1065, 1093, 1094, 1095, 1104, 1108, 1110, 1115, 1116, 1117, 1118, 1130, 1131, 1132, 1133, 1134, 1135, 1143, 1147, 1157, 1158, 1159, 1160, 1161, 1162, 1166, 1167, 2051, 2068, 2071, 2160, 2178, 2180, 2181, 2182, 2183, 3047, 3054, 3057, 3058, 3061, 3062, 3063, 3064, 3067, 3068, 3071, 3072, 3075, 3076, 3087, 3088, 3089, 3090, 3091, 3133, 3156, 3158, 3161, 3167, 3175, 3179, and 3182 are

preferable.

Next, a production process for the compound represented by the general formula [II] of the present invention will be described. The compound represented by the general formula [II] can be produced according to the following Production Process A or B:

Production Process A

This production process is a production process for, of the compounds represented by the general formula [II], the compound represented by the general formula [II-1], [II-2], or [II-3] of the present invention wherein Y is an oxygen atom, a group: $S=O_n$ (wherein n represents an integer of 0 to 2), or a group: NR^9 (wherein R^9 is as defined above) and is characterized by being via an equilibrated mixture of compounds represented by the general formulas [V] and [VI] as production intermediates.

(Step 1)

Carboxylic acid or thiocarboxylic acid represented by the general formula [III]:

[wherein R^0 represents: a substituent selected from the group consisting of a hydrogen atom, an amino group which may be protected, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group which may be protected, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group which may be protected, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an

aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group which may be protected, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; an aryl group which may have one or more substituent(s) selected from the group consisting of a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9

aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, a C_1-C_6 alkylthio group, and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; or a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group; R^{10} and R^{20} are the same or different and each represent: a substituent selected from the group consisting of a hydrogen atom, an amino group which may be protected, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group which may be protected, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group which may be protected, a formyl group, a formylamino group, an aralkyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, a C_2-C_6 alkanoyl

group, an N-C_2-C_6 alkanoylamino group, an aroyl group, an N-aroylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkylthio group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an N-C_1-C_6 alkylamino group, or a C_1-C_6 alkoxy group which may be substituted by the substituent; R^{70} represents a hydrogen atom, or a substituent selected from the group consisting of a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, an aralkyl group, an aralkyloxy group, an aralkylcarbonyl group, an N-aralkylcarbamoyl group, an aryl group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, a C_2-C_6 alkanoyloxy group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6

alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group substituted by R^{80}, and a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group; R^{80} represents a substituent selected from the group consisting of a substituent selected from the group consisting of an azide group, an amino group which may be protected, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group which may be protected, a sulfamoyl group, a sulfo group, a nitro group, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, an N-aroylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N,N-di-C_1-C_{10} alkylcarbamoyl group, an N-C_2-C_6 alkenylcarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group which may be protected, an N-C_1-C_6 alkoxy-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonyl-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6

alkoxycarbonylamino-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_6 alkoxycarbonylamino-C_1-C_6 alkoxycarbonyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group, and a substituent selected from the group consisting of an N-C_1-C_{10} alkylcarbamoyl group and an N-C_1-C_{10} alkylthiocarbamoyl group substituted by the heterocyclic group; X represents an oxygen atom or a sulfur atom; and Z represents: a condensed aryl group; a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group selected from the group consisting of a C_6-C_8 cycloalkanyl group, a C_6-C_8 cycloalkadienyl group, and a C_6-C_8 cycloalkenyl group; or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the bicyclic or tricyclic condensed heteroaromatic group being selected from the group consisting of an ethylenedioxyphenyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a benzimidazolyl group,

a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group] is reacted with an amine derivative represented by the general formula [IV]:

[wherein R^{30}, R^{40}, R^{50}, and R^{60} each independently represent: a substituent selected from the group consisting of a hydrogen atom, an amino group which may be protected, a carbamoyl group, a carbamoylamino group, a carbamoyloxy group, a carboxyl group which may be protected, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group which may be protected, a formyl group, a formylamino group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, a C_3-C_6 cycloalkyloxy group, and an N-C_3-C_6 cycloalkylcarbamoyl group; a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, and a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the substituent; an aryl group which may have one or more substituent(s) selected from the group consisting of a substituent selected from the group consisting of an amino group which may be protected, a carbamoyl group, a

carbamoylamino group, a carbamoyloxy group, a carboxyl group which may be protected, a cyano group, a sulfamoyl group, a sulfo group, a nitro group, a halogen atom, a hydroxy group which may be protected, a formyl group, a formylamino group, an aralkyl group, an N-aralkylamino group, an aralkyloxy group, an N-aralkylcarbamoyl group, an aryl group, an N-arylamino group, an aryloxy group, an arylsulfonyl group, an arylsulfamoyl group, an N-arylcarbamoyl group, an aroyl group, an aroxy group, a C_2-C_6 alkanoyl group, an N-C_2-C_6 alkanoylamino group, an N-C_1-C_6 alkylamino group, an N,N-di-C_1-C_6 alkylamino group, an N-C_1-C_{10} alkylcarbamoyl group, an N-C_1-C_{10} alkylthiocarbamoyl group, an N-amino-C_1-C_{10} alkylcarbamoyl group which may be protected, a C_1-C_6 alkylthio group, an N-C_1-C_6 alkylsulfamoyl group, a C_1-C_6 alkylsulfinyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, an N-C_3-C_6 cycloalkylamino group, and an N-C_3-C_6 cycloalkylcarbamoyl group, and a substituent selected from the group consisting of a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a C_1-C_6 alkoxy group, and an N-C_1-C_6 alkylamino group which may be substituted by the substituent; a monocyclic to tricyclic heteroaromatic group having a 5- or 6-membered heterocyclic group selected from the group consisting of an imidazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group, a thienyl group, a triazolyl group, a pyridyl group, a pyrazinyl group, a pyrimidinyl group, a

pyridazinyl group, a pyrazolyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a dioxanyl group, and a morpholino group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom, the monocyclic to tricyclic heteroaromatic group having 1 to 5 heteroatoms per ring being selected from the group consisting of an ethylenedioxyphenyl group, a dibenzofuranyl group, a dibenzothiophenyl group, a benzimidazolyl group, a benzoxazolyl group, a benzothiazolyl group, a benzotriazolyl group, a benzofuranyl group, and a methylenedioxyphenyl group; or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, or a branched unsaturated C_1-C_9 aliphatic group which may be substituted by the aryl group, the carbocyclic aromatic group, the heterocyclic group, or the heteroaromatic group, or R^{30} and R^{40} or R^{50} and R^{60} together form a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, a 5- or 6-membered saturated carbocyclic group, a 5- or 6-membered unsaturated carbocyclic group, or a 5- or 6-membered heterocyclic group, or R^{30}, R^{40}, R^{50}, and R^{60} together form a condensed aryl group, a bicyclic or tricyclic saturated or unsaturated C_6-C_{15} condensed carbocyclic group, or a bicyclic or tricyclic condensed heteroaromatic group having a 6-membered heterocyclic group or having 1 to 5 heteroatoms per ring selected from the group consisting of a nitrogen atom, an oxygen atom, and a sulfur atom; Y_{10} represents

an oxygen atom, a sulfur atom, or a group: NR^{90} (wherein R^{90} represents a substituent selected from the group consisting of a hydrogen atom, a protective group for the amino group, a hydroxy group which may be protected, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent); and L_{10} represents a hydrogen atom, a protective group for the hydroxy group, a protective group for the mercapto group, or a protective group for the amino group],

and subsequently, when Y_{10} or R^{90} has a protective group for the hydroxy group, a protective group for the mercapto group, or a protective group for the amino group, the protective group is appropriately removed to convert the reaction product to a compound represented by the general formula [V]:

[wherein Y_1 represents an oxygen atom, a sulfur atom, or a group: NR^{90} (wherein R^{90} represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group which may be protected, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group,

a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent); L_1 represents a hydrogen atom; R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, R^{80}, X, and Z are as defined above].

The compound represented by the general formula [V] is in a state equilibrium with a compound represented by the general formula [VI] in a solvent:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, R^{80}, L_1, Y_1, X, and Z are as defined above].

The compounds represented by the general formulas [V] and [VI] are useful as production intermediates of the compound represented by the general formula [II] of the present invention and are usually used as an equilibrated mixture in the reaction.

The equilibrated mixture of the compounds represented by the general formulas [VI] and [VII] wherein Y_1 is an oxygen atom can be converted to an equilibrated mixture of the compounds represented by the general formulas [VI] and [VII] wherein Y_1 is a sulfur atom or a group: NR^{90} (wherein R^{90} represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group which may be protected, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated

C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent), by a method which comprises converting a hydroxy group to a mercapto group or a group: NR^{90} (wherein R^{90} represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group which may be protected, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent), for example, a method which comprises converting a hydroxy group to an azide group through Mitsunobu reaction and then converting the azide group to an amino group by its reduction, or a method which comprises converting a hydroxy group to a methanesulfonyloxy group, which is in turn converted to an acetylmercapto group using potassium thioacetate and then converted to a mercapto group by deacetylation.

A reagent used in the reaction can be increased or decreased appropriately depending on the starting compound and the reaction conditions. Usually, the reaction can be performed by reacting the carboxylic acid or thiocarboxylic acid represented by the general formula [III] with the amine derivative represented by the general formula [IV] at -100°C to the boiling point of the solvent, preferably 0 to 30°C, for 0.5 to 96 hours, preferably 3 to 24 hours,

in the presence of an appropriate base, condensation aid, and/or condensing agent in a dehydrated inert organic solvent. Subsequently, when the condensed compound has a protective group for the amino group, a protective group for the hydroxy group, or a protective group for the mercapto group, the protective group is appropriately removed to complete the reaction.

The inert organic solvent used in the reaction is not particularly limited as long as it does not adversely affect the reaction. Specific examples of the inert organic solvent include methylene chloride, chloroform, 1,2-dichloroethane, trichloroethane, N,N-dimethylformamide, ethyl acetate, methyl acetate, acetonitrile, acetic anhydride, methyl alcohol, ethyl alcohol, benzene, xylene, water, acetic acid, toluene, 1,4-dioxane, and tetrahydrofuran. Particularly, for example, methylene chloride, chloroform, 1,2-dichloroethane, acetonitrile, N,N-dimethylformamide, 1,4-dioxane, and toluene are preferable from the viewpoint of securing the preferable reaction temperature.

Examples of the base used in the reaction include: tertiary aliphatic amines such as trimethylamine, triethylamine, N,N-diisopropylethylamine, N-methylmorpholine, N-methylpyrrolidine, N-methylpiperidine, N,N-dimethylaniline, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and 1,5-azabicyclo[4.3.0]non-5-ene (DBN); aromatic amines such as pyridine, 4-dimethylaminopyridine, picoline, lutidine, quinoline, and isoquinoline; alkali metals such as metal potassium, metal sodium, and metal lithium; alkali metal hydrides such as sodium

hydride and potassium hydride; alkylated alkali metals such as butyllithium; alkali metal alkoxides such as potassium tert-butylate, sodium ethylate, and sodium methylate; alkali metal hydroxides such as potassium hydroxide and sodium hydroxide; and alkali metal carbonates such as potassium carbonate. Among them, for example, tertiary aliphatic amines are preferable. Particularly, for example, triethylamine and N,N-diisopropylethylamine are preferable.

Examples of the condensation aid used in the reaction include N-hydroxybenzotriazole hydrate, N-hydroxysuccinimide, N-hydroxy-5-norbornene-2,3-dicarboximide, and 3-hydroxy-3,4-dihydro-4-oxo-1,2,3-benzotriazole. Among them, for example, N-hydroxybenzotriazole is preferable.

Examples of the condensing agent used in the reaction include thionyl chloride, N,N-dicyclohexylcarbodiimide, 1-methyl-2-bromopyridinium iodide, N,N'-carbonyldiimidazole, diphenylphosphoryl chloride, diphenylphosphoryl azide, N,N'-disuccinimidyl carbonate, N,N'-disuccinimidyl oxalate, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, ethyl chloroformate, isobutyl chloroformate, and benzotriazol-1-yl-oxy-tris(dimethylamino)phosphonium hexafluorophosphate. Among them, for example, N,N-dicyclohexylcarbodiimide, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, ethyl chloroformate, and isobutyl chloroformate are preferable.

The reagent used in the reaction can be increased or decreased

appropriately depending on the starting compound and the reaction conditions. Usually, 0.02 to 50 equivalents, preferably 0.2 to 2 equivalents of the amine derivative represented by the general formula [IV], 1 to 50 equivalents, preferably 3 to 5 equivalents of the base, 1 to 50 equivalents, preferably 1 to 5 equivalents of the condensation aid, and/or 1 to 50 equivalents, preferably 1 to 5 equivalents of the condensing agent are used with respect to the carboxylic acid or thiocarboxylic acid represented by the general formula [III]. These bases, condensation aids, and condensing agents are used alone or in combination of two or more thereof.

(Step 2)

Next, the equilibrated mixture of the compound represented by the general formula [V]:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, R^{80}, L_1, X, Y_1, and Z are as defined above]

and the compound represented by the general formula [VI]:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, R^{80}, L_1, X, Y_1, and Z are as defined above]

is reacted with an acid in an inert organic solvent to form a compound represented by the general formula [VII]:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, R^{80}, X, Y_1, and Z are as defined above],

and subsequently, each protective group present therein can be removed appropriately to produce a compound represented by the general formula [II-1], [II-2], or [II-3]. Moreover, the compound represented by the general formula [VII] wherein Y_1 is a sulfur atom is reacted, for example, with an oxidizing agent such as m-chloroperbenzoic acid for the oxidization of the sulfur atom before or after the appropriate removal of each protective group present therein, and subsequently, the protective group present therein can be removed appropriately to produce a compound represented by the general formula [II-2] wherein Y is a group: $S{=}O_n$ (wherein n represents 1 or 2).

A reagent used in the reaction can be increased or decreased appropriately depending on the starting compound and the reaction conditions. Usually, the reaction can be performed by reacting the equilibrated mixture of the compounds represented by the general formulas [V] and [VI] with a catalytic amount of an acid at -100°C to the boiling point of the solvent, preferably 0 to 30°C, for 0.5 to 96 hours, preferably 2 to 24 hours, in a dehydrated inert organic solvent. Subsequently, when a protective group for the amino group, a protective group for the hydroxy group, or a protective group for the carboxyl group is present, the protective group for the amino group, the protective group for the hydroxy group, or the protective group for the carboxyl group is appropriately removed to complete the reaction.

For protective groups that protect functional groups other than L_{10}, for example, an N-protective group, a protective group

for the carboxyl group, and a protective group for the hydroxy group can also be removed simultaneously by appropriately selecting the types of the protective groups, protective group removal methods, or reaction conditions, etc. Alternatively, any one of an N-protective group, a protective group for the carboxyl group, and a protective group for the hydroxy group can also be removed selectively. Furthermore, the order in which these protective groups are removed is not particularly limited.

Examples of the protective group for the hydroxy group include: lower alkylsilyl groups such as a tert-butyldimethylsilyl group and a tert-butyldiphenylsilyl group; lower alkoxymethyl groups such as a methoxymethyl group and a 2-methoxyethoxymethyl group; aralkyl groups such as a benzyl group and a p-methoxybenzyl group; and acyl groups such as a formyl group and an acetyl group. Particularly, a tert-butyldimethylsilyl group, an acetyl group, and the like are preferable.

Examples of the protective group for the mercapto group include: aralkyl groups such as a benzyl group and a p-methoxybenzyl group; and acyl groups such as a formyl group, a benzoyl group, and an acetyl group. Particularly, a benzoyl group, an acetyl group, and the like are preferable.

Examples of the protective group for the amino group include: aralkyl groups such as a benzyl group and a p-nitrobenzyl group; acyl groups such as a formyl group and an acetyl group; lower alkoxycarbonyl groups such as an ethoxycarbonyl group and a tert-butoxycarbonyl group; and aralkyloxycarbonyl groups such as

a benzyloxycarbonyl group and a p-nitrobenzyloxycarbonyl group. Particularly, a p-nitrobenzyl group, a tert-butoxycarbonyl group, a benzyloxycarbonyl group, and the like are preferable.

Examples of the protective group for the carboxyl group include: lower alkyl groups such as a methyl group, an ethyl group, and a tert-butyl group; and an aralkyl groups such as a benzyl group and a p-methoxybenzyl group. Particularly, a methyl group, an ethyl group, a tert-butyl group, a benzyl group, and the like are preferable.

The removal of each protective group differs depending on the type thereof and the stability of the compound and can be performed according to the method described in the document (see Protective Groups in Organic Synthesis, T.W. Greene, John Wiley & Sons (1981)) or a method equivalent thereto, for example, by solvolysis using an acid or a base, chemical reduction using metal hydride complexes or the like, or catalytic reduction using palladium carbon catalysts, Raney nickel catalysts, or the like.

The inert organic solvent used in the reaction is not particularly limited as long as it does not adversely affect the reaction. Examples thereof include the inert solvent exemplified above.

Examples of the acid used in the reaction include: inorganic acids such as hydrochloric acid, nitric acid, hydrobromic acid, sulfuric acid, hydrofluoric acid, and perchloric acid; Lewis acids such as trifluoroboric acid; sulfonic acids such as p-toluenesulfonic acid, trifluoromethanesulfonic acid, and

methanesulfonic acid; and organic acids such as formic acid, trifluoroacetic acid, and acetic acid. Particularly, for example, Lewis acids such as trifluoroboric acid or organic acids such as trifluoroacetic acid are preferable.

Examples of the oxidizing agent used in the reaction include: inorganic peracids such as hydrogen peroxide; inorganic persalts such as potassium permanganate, sodium hypochlorite, and sodium periodate; and organic peracids such as peracetic acid and m-chloroperbenzoic acid. Particularly, for example, inorganic peracids such as hydrogen peroxide and organic peracids such as m-chloroperbenzoic acid are preferable.

After the completion of the reaction, the product can be further purified by a usual method known in the art to obtain a compound represented by the general formula [II-1], [II-2], or [II-3]. From the reaction solution, the compound represented by the general formula [II-1], [II-2], or [II-3] or a salt thereof can be isolated and purified by separation means known in the art such as solvent extraction, recrystallization, and chromatography.

Production Process B

This production process is a production process for, of the compounds represented by the general formula [II], the compound represented by the general formula [II-1], [II-2], or [II-3] of the present invention wherein Y is an oxygen atom, a group: $S{=}O_n$ (wherein n represents an integer of 0 to 2), or a group: NR^9 (wherein R^9 is as defined above) and is characterized by performing

cyclization without being via the equilibrated mixture of the compounds represented by the general formulas [V] and [VI] as production intermediates.

The carboxylic acid or thiocarboxylic acid represented by the general formula [III]:

[wherein R^0, R^{10}, R^{20}, R^{70}, R^{80}, X, and Z are as defined above]
and a compound represented by the general formula [VIII]:

[wherein Y_2 represents an oxygen atom, a sulfur atom, or a group: NR^{90} (wherein R^{90} is as defined above); L_2 represents a hydrogen atom; and R^{30}, R^{40}, R^{50}, and R^{60} are as defined above]
are reacted with an acid in an inert organic solvent to form a compound represented by the general formula [VII']:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, R^{80}, X, Y_2, and Z are as defined above],
and subsequently, each protective group present therein can be removed appropriately to produce a compound represented by the general formula [II-1], [II-2], or [II-3]. Moreover, the compound represented by the general formula [VII'] wherein Y_2 is a sulfur atom is reacted, for example, with an oxidizing agent such as m-chloroperbenzoic acid for the oxidization of the sulfur atom before or after the appropriate removal of each protective group present therein, and subsequently, the protective group present therein can be removed appropriately to produce a compound

represented by the general formula [II-2] wherein Y is a group: $S{=}O_n$ (wherein n represents 1 or 2).

A reagent used in the reaction can be increased or decreased appropriately depending on the starting compound and the reaction conditions. Usually, the reaction can be performed by reacting the compounds represented by the general formulas [III] and [VIII] with a catalytic amount of an acid at -100°C to the boiling point of the solvent, preferably 0 to 30°C, for 0.5 to 96 hours, preferably 2 to 24 hours, in a dehydrated inert organic solvent. Subsequently, when a protective group for the amino group, a protective group for the hydroxy group, or a protective group for the carboxyl group is present, the protective group for the amino group, the protective group for the hydroxy group, or the protective group for the carboxyl group is appropriately removed to complete the reaction.

For protective groups that protect functional groups, for example, an N-protective group, a protective group for the carboxyl group, and a protective group for the hydroxy group can also be removed simultaneously by appropriately selecting the types of the protective groups, protective group removal methods, or reaction conditions, etc. Alternatively, any one of an N-protective group, a protective group for the carboxyl group, and a protective group for the hydroxy group can also be removed selectively. Furthermore, the order in which these protective groups are removed is not particularly limited.

Examples of the protective group for the hydroxy group include: lower alkylsilyl groups such as a tert-butyldimethylsilyl

group and a tert-butyldiphenylsilyl group; lower alkoxymethyl groups such as a methoxymethyl group and a 2-methoxyethoxymethyl group; aralkyl groups such as a benzyl group and a p-methoxybenzyl group; and acyl groups such as a formyl group and an acetyl group. Particularly, a tert-butyldimethylsilyl, an acetyl group, and the like are preferable.

Examples of the protective group for the amino group include: aralkyl groups such as a benzyl group and a p-nitrobenzyl group; acyl groups such as a formyl group and an acetyl group; lower alkoxycarbonyl groups such as an ethoxycarbonyl group and a tert-butoxycarbonyl group; and aralkyloxycarbonyl groups such as a benzyloxycarbonyl group and a p-nitrobenzyloxycarbonyl group. Particularly, a p-nitrobenzyl group, a tert-butoxycarbonyl group, a benzyloxycarbonyl group, and the like are preferable.

Examples of the protective group for the carboxyl group include: lower alkyl groups such as a methyl group, an ethyl group, and a tert-butyl group; and an aralkyl groups such as a benzyl group and a p-methoxybenzyl group. Particularly, a methyl group, an ethyl group, a tert-butyl group, a benzyl group, and the like are preferable.

The removal of each protective group differs depending on the type thereof and the stability of the compound and can be performed according to the method described in the document (see Protective Groups in Organic Synthesis, T.W. Greene, John Wiley & Sons (1981)) or a method equivalent thereto, for example, by solvolysis using an acid or a base, chemical reduction using metal hydride complexes

or the like, or catalytic reduction using palladium carbon catalysts, Raney nickel catalysts, or the like.

The inert organic solvent used in the reaction is not particularly limited as long as it does not adversely affect the reaction. Examples thereof include the inert solvent exemplified above.

Examples of the acid used in the reaction include: inorganic acids such as hydrochloric acid, nitric acid, hydrobromic acid, sulfuric acid, hydrofluoric acid, and perchloric acid; Lewis acids such as trifluoroboric acid; sulfonic acids such as p-toluenesulfonic acid, trifluoromethanesulfonic acid, and methanesulfonic acid; and organic acids such as formic acid, trifluoroacetic acid, and acetic acid. Particularly, for example, Lewis acids such as trifluoroboric acid or organic acids such as trifluoroacetic acid are preferable.

Examples of the oxidizing agent used in the reaction include: inorganic peracids such as hydrogen peroxide; inorganic persalts such as potassium permanganate, sodium hypochlorite, and sodium periodate; and organic peracids such as peracetic acid and m-chloroperbenzoic acid. Particularly, for example, inorganic peracids such as hydrogen peroxide and organic peracids such as m-chloroperbenzoic acid are preferable.

After the completion of the reaction, the product can be further purified by a usual method known in the art to obtain a compound represented by the general formula [II-1], [II-2], or [II-3]. From the reaction solution, the compound represented by

the general formula [II-1], [II-2], or [II-3] or a salt thereof can be isolated and purified by separation means known in the art such as solvent extraction, recrystallization, and chromatography.

The carboxylic acid or thiocarboxylic acid represented by the general formula [III] is known by documents or can be produced, for example, by reacting carboxylic acid or thiocarboxylic acid which may be protected, represented by the general formula [IX]:

[wherein L_{30} represents a hydrogen atom, a protective group for carboxylic acid, or a protective group for thiocarboxylic acid; and R^0, R^{10}, R^{20}, X, and Z are as defined above]
with a compound represented by the general formula [X]:

$$R^{80}\text{-}R^{70}\text{-}A \qquad [X]$$

[wherein A represents a halogen atom, a leaving group such as a methanesulfonyloxy group or a tributyltin group, or a reactive substituent; and R^{70} and R^{80} are as defined above]
at a low temperature to the boiling point of the solvent in the presence of a base such as potassium carbonate in an appropriate solvent such as acetonitrile or N,N-dimethylformamide, or reacting the compounds at a low temperature to the boiling point of the solvent in the presence of an appropriate base such as potassium carbonate in an appropriate solvent such as toluene and removing the protective group when L_{30} is a protective group for carboxylic acid or a protective group for thiocarboxylic acid).

The compound represented by the general formula [IV] is known by documents and can be produced, for example, by reacting alcohol

or an alcohol derivative represented by the general formula [XI]:

[wherein L_{40} represents a hydrogen atom or a substituent, such as a methanesulfonyl group or a p-toluenesulfonyl group, which is substituted for an oxygen atom to form a leaving group; M_{10} represents a protective group for the amino group; Y_{40} represents an oxygen atom; and R^{30}, R^{40}, R^{50}, and R^{60} are as defined above]

with an amine derivative represented by the general formula [XII]:

$$R^{90}NH\text{-}L_{41} \quad [XII]$$

[wherein L_{41} represents a hydrogen atom or a protective group for the amino group; and R^{90} is as defined above]

or reacting the alcohol or alcohol derivative represented by the general formula [XI] with a mercapto derivative represented by the general formula [XIII]:

$$L_{42}\text{-}SH \quad [XIII]$$

[wherein L_{42} represents a protective group for the mercapto group]

and subsequently removing the protective group when L_{41} or L_{42} is a protective group for the amino group or a protective group for the mercapto group.

Furthermore, a production process for the compound represented by the general formula [I] of the present invention will be described.

The compound represented by the general formula [I] can be produced according to the following Production Process C or D in the same way as the production processes for the compound represented by the general formula [II]:

Production Process C

This production process is a production process for, of the compounds represented by the general formula [I], the compound represented by the general formula [I-1], [I-2], or [I-3] of the present invention wherein Y is an oxygen atom, a group: $S=O_n$ (wherein n represents an integer of 0 to 2), or a group: NR^9 (wherein R^9 is as defined above) and is characterized by being via an equilibrated mixture of compounds represented by the general formulas [V-2] and [VI-2] as production intermediates, as in Production Process A.

(Step 1)

Carboxylic acid or thiocarboxylic acid represented by the general formula [III-2]:

[wherein R^0, R^{10}, R^{20}, R^{70}, X, and Z are as defined above]

is reacted with an amine derivative represented by the general formula [IV]:

[wherein R^{30}, R^{40}, R^{50}, R^{60}, Y_{10}, and L_{10} are as defined above]

in the same way as in Step 1 of Production Process A, and subsequently, when Y_{10} or R^{90} has a protective group for the hydroxy group, a protective group for the mercapto group, or a protective group for the amino group, the protective group is appropriately removed to convert the reaction product to a compound represented by the general formula [V-2]:

[wherein Y_1, L_1, R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, X, and Z are as

defined above].

The compound represented by the general formula [V-2] is in a state equilibrium with a compound represented by the general formula [VI-2] in a solvent:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, L_1, X, Y_1, and Z are as defined above].

The compounds represented by the general formulas [V-2] and [VI-2] are useful as production intermediates of the compound represented by the general formula [I] of the present invention and are usually used as an equilibrated mixture in the reaction.

The equilibrated mixture of the compounds represented by the general formulas [VI-2] and [VII-2] wherein Y_1 is an oxygen atom can be converted to an equilibrated mixture of the compounds represented by the general formulas [VI-2] and [VII-2] wherein Y_1 is a sulfur atom or a group: NR^{90} (wherein R^{90} represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group which may be protected, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, a carbamoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent), by a method which comprises converting a hydroxy group to a mercapto group or a group: NR^{90}

(wherein R^{90} represents a substituent selected from the group consisting of a hydrogen atom, a hydroxy group which may be protected, a formyl group, a C_1-C_6 alkylsulfonyl group, an N-C_1-C_6 alkylsulfonylamino group, a C_1-C_6 alkoxy group, a C_1-C_6 alkoxycarbonyl group, a C_2-C_6 alkanoyl group, a carbamoyl group, and an N-C_1-C_{10} alkylcarbamoyl group, or a linear saturated C_1-C_9 aliphatic group, a linear unsaturated C_1-C_9 aliphatic group, a branched saturated C_1-C_9 aliphatic group, a branched unsaturated C_1-C_9 aliphatic group, or a C_1-C_6 alkylsulfonyl group which may be substituted by the substituent), for example, a method which comprises converting a hydroxy group to an azide group through Mitsunobu reaction and then converting the azide group to an amino group by its reduction, or a method which comprises converting a hydroxy group to a methanesulfonyloxy group, which is in turn converted to an acetylmercapto group using potassium thioacetate and then converted to a mercapto group by deacetylation.

The reagent used in the reaction can be increased or decreased appropriately depending on the starting compound and the reaction conditions. Usually, 0.02 to 50 equivalents, preferably 0.2 to 2 equivalents of the amine derivative represented by the general formula [IV], 1 to 50 equivalents, preferably 3 to 5 equivalents of the base, 1 to 50 equivalents, preferably 1 to 5 equivalents of the condensation aid, and/or 1 to 50 equivalents, preferably 1 to 5 equivalents of the condensing agent are used with respect to the carboxylic acid or thiocarboxylic acid represented by the general formula [III-2]. These bases, condensation aids, and

condensing agents are used alone or in combination of two or more thereof.

(Step 2)

Next, the equilibrated mixture of the compound represented by the general formula [V-2]:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, L_1, X, Y_1, and Z are as defined above]

and the compound represented by the general formula [VI-2]:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, L_1, X, Y_1, and Z are as defined above]

is reacted with an acid in an inert organic solvent in the same way as in Step 2 of Production Process A to form a compound represented by the general formula [VII-2]:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, X, Y_1, and Z are as defined above],

and subsequently, each protective group present therein can be removed appropriately to produce a compound represented by the general formula [I-1], [I-2], or [I-3]. Moreover, the compound represented by the general formula [VII-2] wherein Y_1 is a sulfur atom is reacted, for example, with an oxidizing agent such as m-chloroperbenzoic acid for the oxidization of the sulfur atom before or after the appropriate removal of each protective group present therein, and subsequently, the protective group present

therein can be removed appropriately to produce a compound represented by the general formula [I-2] wherein Y is a group: $S{=}O_n$ (wherein n represents 1 or 2).

A reagent used in the reaction can be increased or decreased appropriately depending on the starting compound and the reaction conditions. Usually, the reaction can be performed by reacting the equilibrated mixture of the compounds represented by the general formulas [V-2] and [VI-2] with a catalytic amount of an acid at -100°C to the boiling point of the solvent, preferably 0 to 30°C, for 0.5 to 96 hours, preferably 2 to 24 hours, in a dehydrated inert organic solvent. Subsequently, when a protective group for the amino group, a protective group for the hydroxy group, or a protective group for the carboxyl group is present, the protective group for the amino group, the protective group for the hydroxy group, or the protective group for the carboxyl group is appropriately removed to complete the reaction.

For protective groups that protect functional groups other than L_{10}, for example, an N-protective group, a protective group for the carboxyl group, and a protective group for the hydroxy group can also be removed simultaneously by appropriately selecting the types of the protective groups, protective group removal methods, or reaction conditions, etc. Alternatively, any one of an N-protective group, a protective group for the carboxyl group, and a protective group for the hydroxy group can also be removed selectively. Furthermore, the order in which these protective groups are removed is not particularly limited.

After the completion of the reaction, the product can be further purified by a usual method known in the art to obtain a compound represented by the general formula [I-1], [I-2], or [I-3]. From the reaction solution, the compound represented by the general formula [I-1], [I-2], or [I-3] or a salt thereof can be isolated and purified by separation means known in the art such as solvent extraction, recrystallization, and chromatography.

Production Process D

This production process is a production process for, of the compounds represented by the general formula [I], the compound represented by the general formula [I-1], [I-2], or [I-3] of the present invention wherein Y is an oxygen atom, a group: $S{=}O_n$ (wherein n represents an integer of 0 to 2), or a group: NR^9 (wherein R^9 is as defined above) and is characterized by performing cyclization without being via the equilibrated mixture of the compounds represented by the general formulas [V-2] and [VI-2] as production intermediates, as in Production Process B.

The carboxylic acid or thiocarboxylic acid represented by the general formula [III-2]:

[wherein R^0, R^{10}, R^{20}, R^{70}, X, and Z are as defined above]

and a compound represented by the general formula [VIII]:

[wherein Y_2, L_2, R^{30}, R^{40}, R^{50}, and R^{60} are as defined above]

are reacted with an acid in an inert organic solvent in the same

way as the reaction of Production Process B to form a compound represented by the general formula [VII'-2]:

[wherein R^0, R^{10}, R^{20}, R^{30}, R^{40}, R^{50}, R^{60}, R^{70}, X, Y_2, and Z are as defined above],

and subsequently, each protective group present therein can be removed appropriately to produce a compound represented by the general formula [I-1], [I-2], or [I-3]. Moreover, the compound represented by the general formula [VII'-2] wherein Y_2 is a sulfur atom is reacted, for example, with an oxidizing agent such as m-chloroperbenzoic acid for the oxidization of the sulfur atom before or after the appropriate removal of each protective group present therein, and subsequently, the protective group present therein can be removed appropriately to produce a compound represented by the general formula [I-2] wherein Y is a group: $S=O_n$ (wherein n represents 1 or 2).

A reagent used in the reaction can be increased or decreased appropriately depending on the starting compound and the reaction conditions. Usually, the reaction can be performed by reacting the compounds represented by the general formulas [III-2] and [VIII] with a catalytic amount of an acid at -100°C to the boiling point of the solvent, preferably 0 to 30°C, for 0.5 to 96 hours, preferably 2 to 24 hours, in a dehydrated inert organic solvent. Subsequently, when a protective group for the amino group, a protective group for the hydroxy group, or a protective group for the carboxyl group is present, the protective group for the amino group, the protective

group for the hydroxy group, or the protective group for the carboxyl group is appropriately removed to complete the reaction.

For protective groups that protect functional groups, for example, an N-protective group, a protective group for the carboxyl group, and a protective group for the hydroxy group can also be removed simultaneously by appropriately selecting the types of the protective groups, protective group removal methods, or reaction conditions, etc. Alternatively, any one of an N-protective group, a protective group for the carboxyl group, and a protective group for the hydroxy group can also be removed selectively. Furthermore, the order in which these protective groups are removed is not particularly limited.

After the completion of the reaction, the product can be further purified by a usual method known in the art to obtain a compound represented by the general formula [I-1], [I-2], or [I-3]. From the reaction solution, the compound represented by the general formula [I-1], [I-2], or [I-3] or a salt thereof can be isolated and purified by separation means known in the art such as solvent extraction, recrystallization, and chromatography.

The carboxylic acid or thiocarboxylic acid represented by the general formula [III-2] is known by documents or can be produced, for example, by reacting aryl halide represented by the general formula [XIV]:

$$R^{70}\text{-}R^{0}\text{-}X \qquad [XIV]$$

[wherein X represents a halogen atom; and R^0 and R^{70} are as defined above]

with metal magnesium at a low temperature to the boiling point of the solvent in an appropriate dehydrated ether solvent such as diethyl ether or tetrahydrofuran and reacting the prepared Grignard reagent with an acid anhydride which may be substituted at a low temperature to room temperature in the dehydrated inert organic solvent.

Moreover, the compound represented by the general formula [III-2] can also be produced by reacting an allene compound represented by the general formula [XV]:

$$R^{70}\text{-}R^{0}\text{-}H \qquad [XV]$$

[wherein R^{0} and R^{70} are as defined above]

with a substituted or unsubstituted acid anhydride through Friedel-Crafts acylation reaction in the presence of the appropriate acid.

Next, to specifically show the usefulness of the present invention, a compound of Example 38 was evaluated as a typical compound for its influence to GLP-1 concentrations in plasma after administration. The test method and results are shown below.

(Test method)

Male Wister rats (8 week old, n=6) raised under free eating and drinking conditions were fasted from noon of the day before the test. To the rats, the compound suspended in a 1% carboxymethylcellulose solution was administered. As a control group, a 1% carboxymethylcellulose solution was orally administered to the rats. 30 minutes after the test drug administration, blood was collected, and plasma was separated from the obtained blood

by centrifugation. GLP-1 concentrations in the plasma were quantified by radioimmunoassay using commercially available anti-GLP-1 antibodies (COSMO BIO Co., Ltd.). The obtained numeric values were analyzed using the Student's T test to calculate the statistically significant difference thereof. The results are shown in Table 45 below.

(Test results)

Table 45

#1 Plasma GLP-1 concentration

#2 Control group

#3 Compound group

From these results, a significantly high value of GLP-1 in plasma was confirmed in the plasma of the 0.3 mg/kg compound-administered group 30 minutes after the administration, compared with that of the control group. This result demonstrated that the compound of the present invention has an activity that can achieve a high GLP-1 concentration in blood in rats.

The compound of the present invention exhibits an activity that achieves a high GLP-1 concentration in blood and is thus useful as a therapeutic agent for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug.

The compounds represented by the general formulas [I] and [II] of the present invention can be used as a pharmaceutical drug, particularly, a therapeutic agent for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug, comprising the same as an active ingredient. The

compound of the present invention in such a pharmaceutical drug, particularly, a therapeutic agent for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug means pharmaceutically acceptable general-purpose compounds and encompasses, for example, a compound represented by the general formula [II]:

[wherein R, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, X, Y, and Z are as defined above],

a pharmaceutically acceptable ester or salt of the carboxyl group on R, R^1, R^2, R^3, R^4, R^5, R^6, or R^8, a salt of the hydroxy group on R, R^1, R^2, R^3, R^4, R^5, R^6, or R^8, or a salt of the an amino group on R, R^1, R^2, R^3, R^4, R^5, R^6, or R^8.

Examples of the salt of the carboxyl group or the hydroxy group include: alkali metal salts such as sodium salt and potassium salt; and alkaline-earth metal salts such as calcium salt and magnesium salt.

Examples of acid-addition salts of the amino group include: inorganic acid salts such as hydrochloride, sulfate, nitrate, phosphate, carbonate, bicarbonate, and perchlorate; organic acid salts such as acetate, propionate, lactate, maleate, fumarate, tartrate, malate, citrate, and ascorbate; sulfonates such as methanesulfonate, isethionate, benzenesulfonate, and toluenesulfonate; and acidic amino acid salts such as aspartate and glutamate.

When the compound of the present invention is used as a

therapeutic agent for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug, it can also be used as a pharmaceutically acceptable salt. Typical examples of the pharmaceutically acceptable salt can include salts with alkali metals such as sodium and potassium.

A production process for the pharmaceutically acceptable salt of the compound of the present invention can be performed by appropriately combining methods usually used in the field of organic synthetic chemistry. Specific examples thereof include the neutralization and titration of a solution of the compound of the present invention in a free form using an alkali solution.

The dosage form of the compound of the present invention used as a therapeutic agent for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug can be selected from among various forms. Examples thereof include: oral formulations such as tablets, capsules, powders, granules, and liquid formulations; and sterilized liquid parenteral formulations such as solutions and suspensions.

Solid preparations can also be produced directly in the form of tablets, capsules, granules, or powders or produced using appropriate additives. Examples of the additives include: sugars such as lactose and glucose; starches such as corn, wheat, and rice; fatty acids such as stearic acid; inorganic salts such as sodium metasilicate, magnesium aluminate, and anhydrous calcium phosphate; synthetic polymers such as polyvinyl pyrrolidone and polyalkylene glycol; fatty acid salts such as calcium stearate and

magnesium stearate; alcohols such as stearyl alcohol and benzyl alcohol; synthetic cellulose derivatives such as methylcellulose, carboxymethylcellulose, ethylcellulose, and hydroxypropylmethylcellulose; and other additives usually used, such as water, gelatin, talc, plant oils, and gum arabic.

These solid preparations such as tablets, capsules, granules, and powders can generally comprise 0.1 to 100% by weight, preferably 5 to 100% by weight of the active ingredient. Liquid preparations can be produced in the form of suspensions, syrups, injections, and the like using water, alcohols, or appropriate additive usually used in liquid preparations, such as plant-derived oils, for example, soybean oil, peanut oil, and sesame oil. Particularly, examples of solvents appropriate for parenteral administration include injectable distilled water, an aqueous lidocaine hydrochloride solution (for intramuscular injection), saline, an aqueous glucose solution, ethanol, liquids for intravenous injection (e.g., aqueous solutions of citric acid or sodium citrate), and electrolyte solutions (e.g., for intravenous drips or intravenous injection), and mixed solutions thereof.

Moreover, the liquid formulations for oral administration such as suspensions or syrups can comprise 0.5 to 10% by weight of the active ingredient.

The actually preferable dose of the compound of the present invention can be increased or decreased appropriately depending on the type of the compound used, the type of a composition in which the compound is formulated, application frequency, a particular

site to be treated, and the symptoms of a patient. For example, the daily dose in adult is 0.1 to 1000 mg for oral administration and is 0.01 to 500 mg for parenteral administration. The number of doses differs depending on an administration method and symptoms, and the compound of the present invention can be administered in one portion or in 2 to 5 divided portions.

Best Mode for Carrying Out the Invention

The present invention will be described more specifically with reference to Examples. However, the present invention is not intended to be limited to them by any means.

In thin-layer chromatography of Examples, Silica gel $60F_{245}$ (Merck KGaA) was used as a plate, and a UV detector was used as a detection method. Wakogel™ C-300 (Wako Pure Chemical Industries, Ltd.) was used as a silica gel for columns, and LC-SORB™ SP-B-ODS (Chemco Scientific Co., Ltd.) or YMC-GEL™ ODS-AQ 120-S50 (Yamamura Chemical Laboratories, Co., Ltd.) was used as a silica gel for reverse-phase columns.

i-Bu: isobutyl group

n-Bu: n-butyl group

t-Bu: t-butyl group

Me: methyl group

Et: ethyl group

Ph: phenyl group

i-Pr: isopropyl group

n-Pr: n-propyl group

$CDCl_3$: deuterated chloroform

methanol-d_4: deuterated methanol

DMSO-d_6: deuterated dimethyl sulfoxide

Example 1

Production of compound No. 1134

2-(4-(3-isopropyl-5-oxo-2-phenyl-2,3-dihydro[1,3]oxazolo[2,3-a]isoindol-9b(5H)-yl)-2-methylphenoxy)-N-propylacetamide:

(compound of the general formula [II-1] wherein R^1: H; R^2: H; R^3: i-Pr; R^4: H; R^5: Ph; R^6: H; R^7: 4-CH_2O; R^8: n-PrNHCO; X: O; Y: O; Z: Ph; R: 3-Me-Ph)

To a tetrahydrofuran solution (250 ml) containing 11.0 g (74.0 mmol) of phthalic anhydride, a tetrahydrofuran solution (250 ml) of a Grignard reagent prepared from 2.71 g (110 mmol) of magnesium and 22.4 g (110 mmol) of 4-bromo-2-methylanisole was added dropwise at -70°C over 30 minutes in a nitrogen atmosphere. The reaction solution was stirred at -70°C for 2 hours. Then, to the reaction solution, a saturated aqueous solution of ammonium chloride was added. The reaction solution was subjected to extraction with ethyl acetate, and the organic layer was washed with saturated saline, then dried, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=1:1) to obtain 8.98 g of 2-(4-methoxy-3-methylbenzoyl)benzoic acid (yield: 45%) as a white solid.

1.00 g (3.70 mmol) of 2-(4-methoxy-3-methylbenzoyl)benzoic

acid was dissolved in a 10% hydrochloric acid-methanol solution (20 ml). The reaction solution was stirred at room temperature for 12 hours and then concentrated under reduced pressure to obtain 1.05 g of semi-purified methyl 2-(4-methoxy-3-methylbenzoyl)benzoate (yield: 100%).

To a methylene chloride solution (25 ml) containing 1.00 g (3.52 mmol) of methyl 2-(4-methoxy-3-methylbenzoyl)benzoate, a 1 N methylene chloride solution (18 ml) of boron tribromide was added under ice cooling, and the reaction solution was stirred at room temperature for 12 hours. To the reaction solution, methanol (18 ml) and water were added, followed by extraction with chloroform. The organic layer was washed with saturated saline, dried, and concentrated under reduced pressure. The obtained residue was dissolved in 10% hydrochloric acid-methanol (15 ml). The reaction solution was stirred at room temperature for 12 hours and then concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=7:3) to obtain 670 mg of methyl 2-(4-hydroxy-3-methylbenzoyl)benzoate (yield: 70%) as a white solid.

To an acetonitrile solution (4 ml) containing 660 mg (2.44 mmol) of methyl 2-(4-hydroxy-3-methylbenzoyl)benzoate and 840 mg (6.10 mmol) of potassium carbonate, an acetonitrile solution (4 ml) of 2-bromo-N-propylacetamide (3.66 mmol) was added at room temperature, and the reaction solution was stirred at room temperature for 12 hours. To the reaction solution, ethyl acetate

and water were added, and the organic layer was washed with saturated saline, dried, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=1:1) to obtain 868 mg of methyl 2-(3-methyl-4-(2-oxo-2-(propylamino)ethoxy)benzoyl)benzoate (yield: 96%) as a pale yellow oil.

To a methanol solution (10 ml) containing 860 mg (2.33 mmol) of methyl 2-(3-methyl-4-(2-oxo-2-(propylamino)ethoxy)benzoyl)benzoate, a 4 N sodium hydroxide solution (2.3 ml) was added at room temperature, and the reaction solution was stirred at room temperature for 2.5 hours. To the reaction solution, a 1 N aqueous hydrochloric acid solution (15 ml) was added, followed by extraction with ethyl acetate. The organic layer was washed with saturated saline, dried, and concentrated under reduced pressure. The obtained residue was subjected to 3 repetitive runs of azeotropy with toluene and concentrated under reduced pressure to obtain 820 mg of 2-(3-methyl-4-(2-oxo-2-(propylamino)ethoxy)benzoyl)benzoic acid (yield: 99%) as a white solid.

To a methylene chloride solution (1 ml) containing 48.0 mg (0.14 mmol) of 2-(3-methyl-4-(2-oxo-2-(propylamino)ethoxy)benzoyl)benzoic acid, 21.5 mg (0.12 mmol) of (2R)-2-amino-3-methyl-1-phenylbutan-1-ol and 0.043 ml (0.31 mmol) of triethylamine, 22.0 mg (0.16 mmol) of 1-hydroxybenzotriazole hydrate and 31.0 mg (0.16 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride were

added at room temperature, and the reaction solution was stirred at room temperature for 12 hours. To the reaction solution, water was added, followed by extraction with chloroform. The organic layer was washed with saturated saline, dried, and concentrated under reduced pressure. The obtained unpurified alcohol was dissolved in methylene chloride (2 ml). To the solution, trifluoroacetic acid (1 ml) was added at room temperature, and the reaction solution was stirred at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure. Then, the obtained residue was subjected to 3 repetitive runs of azeotropy with toluene and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=1:1) to obtain 18.0 mg of the title compound (yield: 29%) as a pale yellow oil.

[NMR1]

Compounds of the general formula [I-1] or [II-1] of compound Nos. 1001 to 1024, 1028, 1034 to 1042, 1045, 1062, 1065, 1093, 1094, 1095, 1104, 1108, 1110, 1115 to 1118, 1130 to 1133, 1135, 1143, 1147, 1157 to 1162, 1166, and 1167 in the compound list were obtained in the same way as in Example 1. Their physical constants are shown below.

Example 2

Example 64

Production of compound No. 2071

2-(4-(3-isopropyl-5-oxo-2,3-dihydro[1,3]thiazolo[2,3-a]isoindo l-9b(5H)-yl)-2-methylphenoxy)-N-propylacetamide: (compound of the general formula [II-2] wherein R^1: H; R^2: H; R^3: i-Pr; R^4: H; R^5: Ph; R^6: H; R^7: 4-CH_2O; R^8: n-PrNHCO; X: O; Y: S; Z: Ph; R: 3-Me-Ph)

To a methanol solution (1 ml) containing 42.0 mg (0.16 mmol) of S-(2-((t-butoxycarbonyl)amino)-3-methylbutyl)ethanethioate, a 1 N aqueous sodium hydroxide solution (0.18 ml) was added under ice cooling, and the reaction solution was stirred at room temperature for 15 minutes and then concentrated under reduced pressure. The obtained residue and 63.0 mg (0.18 mmol) of 2-(3-methyl-4-(2-oxo-2-(propylamino)ethoxy)benzoyl)benzoic acid were dissolved in toluene (5 ml). To the solution, 37.0 mg (0.19 mmol) of p-toluenesulfonic acid monohydrate was added at room temperature, and the reaction solution was stirred at 160°C for 30 minutes. After addition of water and ethyl acetate, the organic layer was dried and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=1:2) and preparative high-performance liquid chromatography (hexane:isopropanol=55:45) to obtain 7.0 mg (yield: 10%) of a diastereomer A and 1.0 mg (yield: 1%) of a diastereomer B of the title compound as pale yellow oils.

Diastereomer A

[NMR2]

Example 72

Production of compound No. 2160 (R^1: H; R^2: H; R^3, R^4, R^5, and R^6: Ph (R^3, R^4, R^5, and R^6 together form a Ph group); R^7: 4-CH_2O; R^8: n-PrNHCO; X: O; Y: S; Z: Ph; R: 3-Me-Ph)

[NMR3]

Example 73

Production of compound No. 2178

2-(4-(3-isopropyl-1-oxido-5-oxo-2,3-dihydro[1,3]thiazolo[2,3-a]isoindol-9b(5H)-yl)-2-methylphenoxy)-N-propylacetamide:

(compound of the general formula [II-2] wherein R^1: H; R^2: H; R^3: i-Pr; R^4: H; R^5: Ph; R^6: H; R^7: 4-CH_2O; R^8: n-PrNHCO; X: O; Y: S=O; Z: Ph; R: 3-Me-Ph)

To a methylene chloride solution (1 ml) containing 5.00 mg (0.011 mmol) of 2-(4-(3-isopropyl-5-oxo-2,3-dihydro[1,3]thiazolo[2,3-a]isoindol-9b(5H)-yl)-2-methylphenoxy)-N-propylacetamide (diastereomer A of Example 64), 10.0 mg (0.057 mmol) of m-chloroperbenzoic acid was added under ice cooling in a nitrogen atmosphere, and the reaction solution was stirred for 1 hour under ice cooling. To the reaction solution, a saturated aqueous solution of sodium thiosulfate was added, and the reaction solution was stirred for 5 minutes. After addition of a saturated aqueous solution of sodium chloride and ethyl acetate, the organic layer was dried and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=1:2) and preparative high-performance liquid

chromatography (hexane:isopropanol=55:45) to obtain 1.8 mg of the title compound (yield: 35%) as a pale yellow oil.

[NMR4]

Example 74

Production of compound No. 2181

2-(4-(3-isopropyl-1,1-dioxido-5-oxo-2,3-dihydro[1,3]thiazolo[2,3-a]isoindol-9b(5H)-yl)-2-methylphenoxy)-N-propylacetamide: (compound of the general formula [II-2] wherein R^1: H; R^2: H: R^3: i-Pr; R^4: H; R^5: Ph; R^6: H; R^7: 4-CH_2O; R^8: n-PrNHCO; X: O; Y: $S=O_2$; Z: Ph; R: 3-Me-Ph)

To a methylene chloride solution (1 ml) containing 5.00 mg (0.011 mmol) of 2-(4-(3-isopropyl-5-oxo-2,3-dihydro[1,3]thiazolo[2,3-a]isoindol-9b(5H)-yl)-2-methylphenoxy)-N-propylacetamide (diastereomer A of Example 64), 10.0 mg (0.057 mmol) of m-chloroperbenzoic acid was added under ice cooling in a nitrogen atmosphere, and the reaction solution was stirred for 1 hour under ice cooling. To the reaction solution, a saturated aqueous solution of sodium thiosulfate was added, and the reaction solution was stirred for 5 minutes. After addition of a saturated aqueous solution of sodium chloride and ethyl acetate, the organic layer was dried and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=1:2) and preparative high-performance liquid chromatography (hexane:isopropanol=55:45) to obtain 3.2 mg of the

title compound (yield: 60%) as a pale yellow oil.

[NMR5]

Compounds of the general formula [I-2] or [II-2] of compound Nos. 2047, 2048, 2049, 2050, 2180, 2182, and 2183 in the compound list were obtained in the same way as in Example 74. Their physical constants are shown below.

Example 75

Example 82

Production of compound No. 3067

2-(4-(3-isopropyl-5-oxo-2,3-dihydro-1H-imidazo[2,1-a]isoindol-9b(5H)-yl)-2-methylphenoxy)-N-propylacetamide: (compound of the general formula [II-3] wherein R^1: H; R^2: H; R^3: i-Pr; R^4: H; R^5: H; R^6: H; R^7: 4-CH_2O; R^8: n-PrNHCO; R^9: H; X: O; Y: N; Z: Ph; R: 3-Me-Ph)

To a methylene chloride solution (15 ml) containing 400 mg (1.10 mmol) of 2-(3-methyl-4-(2-oxo-2-(propylamino)ethoxy)benzoyl)benzoic acid, 200 mg (1.00 mmol) of t-butyl 2-amino-3-methylbutylcarbamate, and 0.41 ml (3.00 mmol) of triethylamine, 227 mg (1.20 mmol) of 1-hydroxybenzotriazole hydrate and 160 mg (1.20 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride were added at room temperature, and the reaction solution was stirred at room temperature for 12 hours. To the reaction solution, a 1 N aqueous hydrochloric acid solution was added, followed by

extraction with ethyl acetate. The organic layer was washed with saturated saline, then dried, and concentrated under reduced pressure. The obtained unpurified condensed product was dissolved in methylene chloride (5 ml). To the solution, trifluoroacetic acid (5 ml) was added at room temperature, and the reaction solution was stirred at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure. Then, the obtained residue was subjected to 3 repetitive runs of azeotropy with toluene and concentrated under reduced pressure. The obtained residue was dissolved in toluene (5 ml). To the solution, p-toluenesulfonic acid monohydrate (20 mg) was added, and the mixture was stirred at 140°C for 6 hours. To the reaction solution, a saturated aqueous solution of sodium bicarbonate (10 ml) was added, followed by extraction with ethyl acetate. The organic layer was washed with saturated saline, then dried, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=1:2) to obtain 232 mg of the title compound (yield: 55%) as a pale yellow oil.

[NMR6]

2-(4-(3-isopropyl-5-oxo-2,3-dihydro-1H-imidazo[2,1-a]isoindol-9b(5H)-yl)-2-methylphenoxy)-N-propylacetamide hydrochloride (hydrochloride of the compound of Example 82)

2-(4-(3-isopropyl-5-oxo-2,3-dihydro-1H-imidazo[2,1-a]isoindol-9b-yl)-2-methylphenoxy)-N-propylacetamide (compound of Example 82) was dissolved in a hydrochloric acid-dioxane solution

(10 ml) and stirred at room temperature for 1 hour. The reaction solution was concentrated under reduced pressure. Then, the obtained residue was subjected to 3 repetitive runs of azeotropy with toluene and concentrated under reduced pressure. The obtained residue was crystallized from chloroform-hexane to obtain 140 mg of the title compound (yield: 62%) as a white solid.

Compounds of the general formula [I-3] or [II-3] of compound Nos. 3001, 3014, 3025 to 3033, 3036, 3038, 3039, 3046, 3047, 3054, 3057, 3058, 3061 to 3064, 3068, 3071, 3072, 3075, 3076, 3087 to 3091, 3133, 3156, 3158, 3161, 3167, 3175, 3179, and 3182 in the compound list were obtained in the same way as in Example 82. Their physical constants are shown below.

Example 83

Example 123

Formulation Examples

Hereinafter, Formulation Examples of the compound of the present invention will be shown. However, the formulation of the compound of the present invention is not intended to be limited to these Formulation Examples.

Formulation Example 1

Compound of compound no. 106745 parts

Heavy magnesium oxide 15 parts

Lactose	75 parts

These ingredients were uniformly mixed to form powders in a powdery or fine granular form of 350 μm or smaller. These powders were charged into capsule shells to form capsules.

Formulation Example 2

Compound of compound no. 30674	5 parts
Starch	15 parts
Lactose	16 parts
Crystalline cellulose	21 parts
Polyvinyl alcohol	3 parts
Distilled water	30 parts

These ingredients were uniformly mixed, then pulverized, and granulated. After drying, the powders were sifted to form granules of 141 to 177 μm in size.

Formulation Example 3

Granules were prepared in the same way as in Formulation Example 2. Then, to 96 parts of the granules, 4 parts of calcium stearate were added. The mixture was compression-molded to prepare tablets of 10 mm in diameter.

Formulation Example 4

To 90 parts of granules obtained by the method of Formulation Example 2, 10 parts of crystalline cellulose and 3 parts of calcium stearate were added. The mixture was compression-molded to prepare

tablets of 8 mm in diameter. Then, a mixed suspension of syrup gelatin and precipitated calcium carbonate was added thereto to prepare sugar-coated tablets.

Industrial Applicability

An isoindole derivative as a compound of the present invention exhibits an activity that achieves a high GLP-1 concentration in blood and is thus useful as a therapeutic agent for diabetes mellitus, a preventive agent for chronic diabetic complications, or an antiobesity drug.